APPLICATIONS OF ZEOLITES

TO ORGANIC SYNTHESIS

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ABSTRACT

The application of zeolites as catalysts for a number of organic, liquid-phase, acid-promoted reactions is discussed with reference to zeolite acidity and structure on product yield and selectivity. The zeolites described are predominantly high silica materials including Nu-2, ZSM-5, Nu-10 and EU-1 structures.

Examination of the Claisen rearrangement of allyl phenyl ether has shown that it is promoted by zeolites relative to the thermal reaction and that the extent of conversion increases with zeolite acidity. In addition to the expected products, 2-allylphenol and the cyclic 2-methyldihydrobenzofuran, small quantities of the para-product, 4-allylphenol, are detected over H-Nu-2 and (Cu(II),H)-Y zeolites. 4-Allylphenol is not detected in the thermal rearrangement and its formation in the present work is attributed to an intermolecular mechanism via ether cleavage.

Also examined is the Fries rearrangement of phenyl acetate and phenyl benzoate. The product selectivity is compared with that over Nafion-H, an acidic, non-porous, perfluorinated ion-exchange resin. Both rearrangements are more para- selective when performed in the presence of zeolites. In the rearrangement of phenyl acetate a number of by-products in addition to the expected 2- and 4- hydroxyacetophenones are observed.

The aldol self-condensation of acetophenone to yield β-methylchalcone and of acetophenone and benzaldehyde to yield chalcone is promoted by H-Nu-2 zeolite. The ring closure of 2-benzoylbenzoic acid to anthraquinone takes place quantitatively over H-Nu-2. The cyclisation is monitored by i.r. to completion and the product isolated by extraction or sublimation.

Of those zeolites examined, H-Nu-2 is likely to be most widely applicable as a catalyst in organic synthesis because of its relatively large pore dimensions, high silica content (thermal stability) and high acidity.

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POST GRADUATE LECTURES

The following post-graduate lecture courses were attended during 1985 and 1988.

- N.m.r. (Dr. Sadler), five lectures.
- Mass Spectrometry (Prof. K. R. Jennings), five lectures.
- Catalysis and the Chemical Industry (various lecturers), five lectures.
- Medicinal Chemistry (Prof. Sammes), five lectures.
- Industrial Chemistry (various lecturers), five lectures.
- Developments in Organic Chemistry (various lecturers), five lectures.
- Departmental Seminars - three years' attendance.
- Departmental Zeolite Group Meetings - three years' attendance

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GLOSSARY OF TERMS, SYMBOLS AND ABBREVIATIONS

A	angstroms (10^{-10}m)
a.a.s.	atomic absorption spectroscopy
2-AAP	2-acetoxyacetophenone
4-AAP	4-acetoxyacetophenone
2-AP	2-allylphenol
4-AP	4-allylphenol
APE	allyl phenyl ether
AQ	anthraquinone
2-BBA	2-benzoylbenzoic acid
b.p.	boiling point
δ	chemical shift
ϵ	extinction coefficient
g.c.	gas chromatography
g.c.-m.s.	gas chromatography - mass spectroscopy
h	hour
2-HAP	2-hydroxyacetophenone
4-HAP	4-hydroxyacetophenone
2-HBP	2-hydroxybenzophenone
4-HBP	4-hydroxybenzophenone
h.p.l.c.	high performance liquid chromatography
i.r.	infra-red
J	coupling constant
m	multiplet
M	molar
min	minute
m.p.	melting point
m/z	mass to charge ratio
ν max	wavenumber of absorbance maximum (i.r.)

n.m.r.	nuclear magnetic resonance
NOE	nuclear Overhauser enhancement
pa	phenyl acetate
ph	phenol
p.p.m.	parts per million
q	quartet
s	singlet
s.e.m.	scanning electron microscopy
t	triplet
t.g.a.	thermal gravimetric analysis
t.l.c.	thin-layer chromatography
tot	total
u.v.	ultra-violet
w/w	weight for weight
x.r.d.	x-ray diffraction (powder)

1. INTRODUCTION

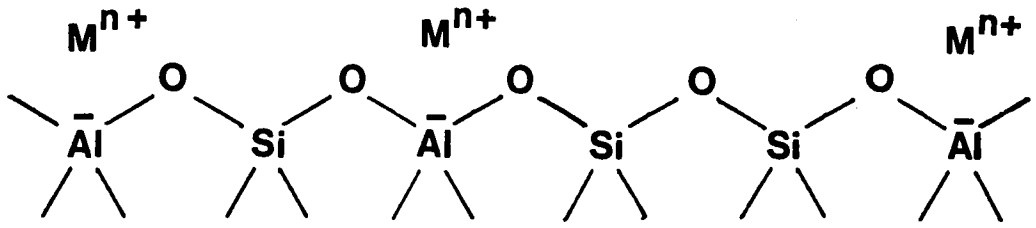
Zeolites are crystalline aluminosilicates with a well-defined porous structure[1]. Within the framework is a system of channels or cages occupied by cations and water molecules. The typical diameter of these cavities is 2-13 angstroms (Å), thus they are of molecular dimensions. A combination of strong acid sites and shape-selectivity[2] for reactions within the channels has led to the important use of zeolites as catalysts in the oil and petrochemical industries[3], e.g. in Fluid Catalytic Cracking (FCC) and <u>para</u>-selective isomerisation of aromatics. The same properties also offer significant potential to organic synthesis.

The chemical composition of zeolites corresponds to the general formula:

$$M^{n+}_{x/n} [(AlO_2^-)x \ (SiO_2)y]w.\ H_2O$$

The three-dimensional network is formed by the linkage of (SiO_4) and (AlO_4) tetrahedra through single, shared oxygen. As Si is tetravalent and Al is trivalent there is a net negative charge balanced by a cation M^{n+} (Figure 1). These charge-compensating cations readily undergo reversible ion-exchange.

Figure 1



The tetrahedra form rings, usually containing between 4-12 tetrahedral units (T-atom rings) which define the diameter of the entrances to channels or cages. Thus, molecules larger than this aperture are restricted from diffusion into the zeolite (although molecules with dimensions slightly too large may pass through because of molecular vibration).

The zeolites which have been employed in this work illustrate the range of channel size and structure available and are detailed in Table 1. Of these, the faujasite, Mordenite and A structures are well-known and well-characterised[1], and have a relatively low silica content. The more recent development of the high silica zeolites in the last two decades has provided many new framework structures.

Table 1 Zeolite Structures

zeolite	classification (pore-size)	structure type	type of access (dimensions/ T-ring)	limiting aperture (Å)	supercage (Å)	typical Si/Al
X,Y[1]	Large-pore	FAU	3D - 12,12,12	7.4	13	1.5-3
Nu-2(β)[5]	Large		3D - 12,12,12	8	-	13
Mordenite[1]	Large	MOR	2D - 8,12	6.7x7.0 2.9x5.7	-	4.5-5
ZSM-5[6-8]	Medium	MFI	3D - 10,10,10	5.1x5.5 5.4x5.6	-	>40
Nu-10[9-12]	Medium	TON	1D - 10	5.4x4.5	-	45
EU-1[13-15]	Medium	EUO	1D - 10	5.8x4.1	-	20
A[1]	Small	LTA	3D - 8,8,8	4.2	11	1.0-1.2
$AlPO_4$-5[16]	Large	AFI	1D - 12,12,12	8	-	-

Zeolites (Table 1) can be classified as large, medium or small pore on the basis of the limiting channel size for molecular diffusion into the framework. Thus, zeolite Y (large pore) has the three-dimensional faujasite structure (Figure 2). The main channels are defined by 12-T atom rings of diameter 7.4Å which intersect at a supercage of cross-section 13Å. However, entrance to the supercage is limited by the 12-T atom windows.

In contrast, the high silica ZSM-5 contains no supercages. This zeolite is a medium pore material which possess two types of channels, both of which are composed of 10-T atom rings (Figure 3). One channel system is sinusoidal with a nearly circular cross-section of 5.5Å and the other is straight and perpendicular to the sinusoidal system with elliptical pores 5.1 x 5.5Å diameter. Zeolite Nu-10, another high-silica, medium pore material has only one-dimensional channels, defined by 10-T atom rings (Figure 4).

The small-pore structures, e.g. zeolite A, have windows which are too small for sorption of aromatic molecules. Benzene has a kinetic diameter of 5.85Å whereas the channels of A have 8-T atom windows for diameter 4.1Å which intersect at a supercage of cross-section 11Å.

Figure 2 Faujasite (X,Y) framework structure

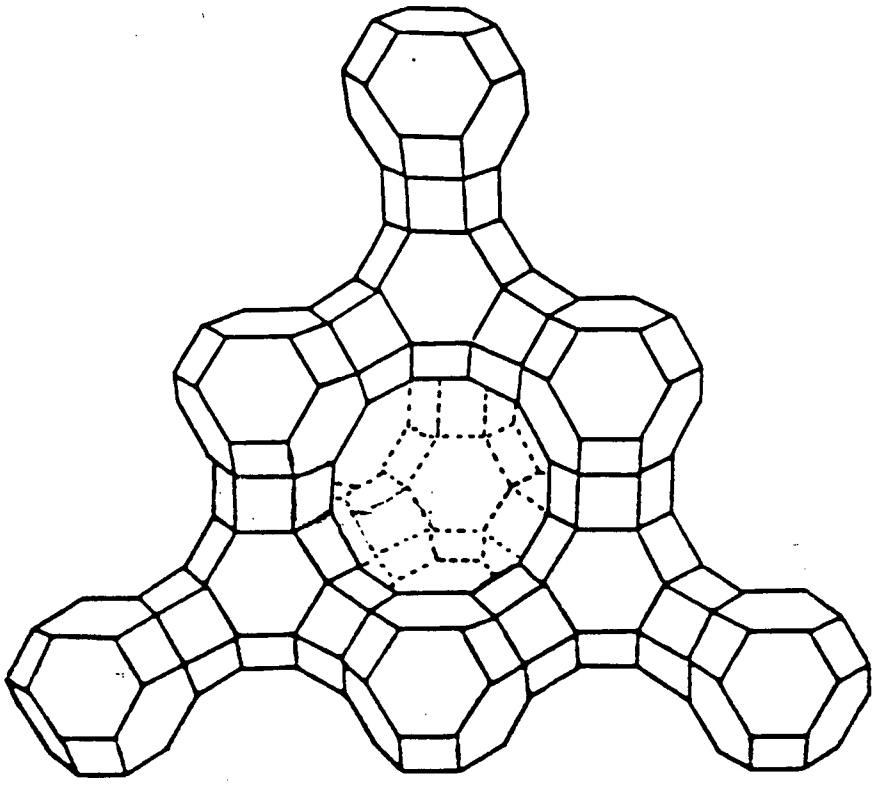


Figure 3 ZSM-5 framework structure

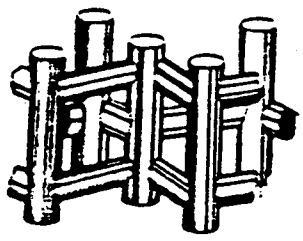
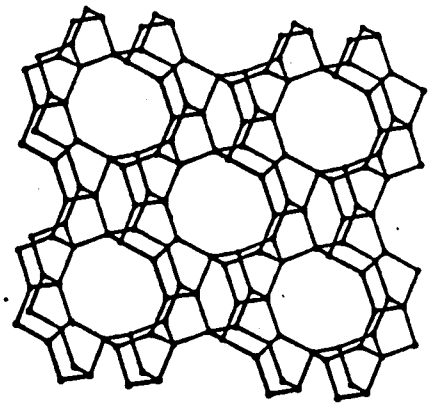


Figure 4 Nu-10 framework structure

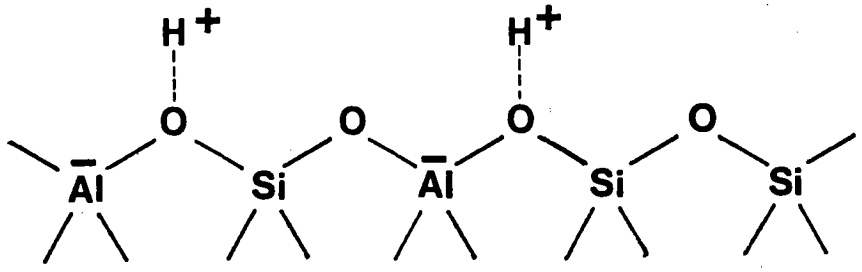


Zeolite structure types are assigned a IUPAC three letter code by the International Zeolite Structure Commission[4] (Table 1). Thus materials with the same framework structure, although not necessarily synthesised by the same method or with the same Si/Al ratio are given the same code.

Zeolites are generally synthesised hydrothermally under alkaline conditions[17]. Silica, alumina and metal cation sources in solution form an amorphous gel which eventually crystallises into the framework structure. The synthesis conditions can be critical. The structure formed may depend on the reactant source and purity, the chemical composition, reaction time and extent of agitation. The newer, high silica zeolites[18] often require higher temperatures and pressures, and are usually synthesised in the presence of quaternary ammonium salts, e.g. tetra-n-propylammonium salts for ZSM-5. These appear to function partly as templates for the channel system, but their role has not been entirely clarified. After synthesis, the organic material can be removed from the channels by calcination.

Both Bronsted and Lewis acid sites are found in zeolites. Bronsted acid sites are associated with aluminium in the framework and are attributed to bridged hydroxyl groups in the channels[19]. (Figure 5).

Figure 5



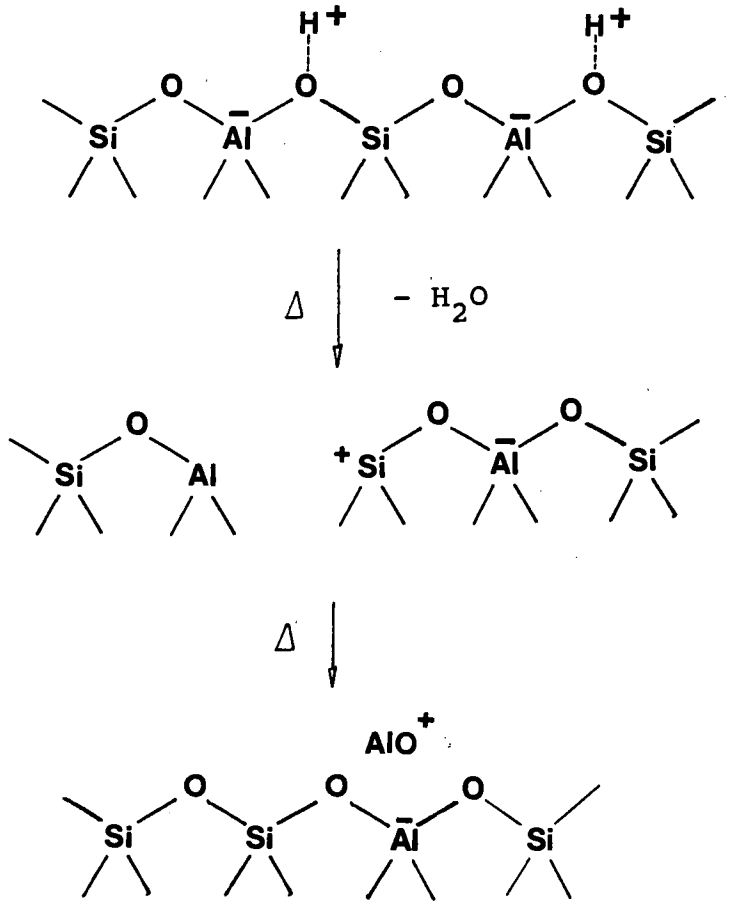
The Si/Al ratio has an important effect on acidity. It has been shown that the rate of acid-catalysed reactions, e.g. n-hexane cracking and isomerisation of cyclopropane increases rapidly as Si/Al is raised from 2.5 to 6[19]. This is attributed to increased strength of the acid sites, through weakening of the hydroxyl bond by electrostatic effects. At Si/Al > 6, the rate of these reactions decreases and can be correlated with the decline in the number of Al atoms. Thus at high Si/Al (>7) aluminium sites are isolated, ie. no proximate aluminium atoms and these sites will be of common acidity.

Under the conditions employed in the present work it is assumed that Bronsted sites are predominant in the activity. Thus the relative acidity of a series of zeolites can be roughly correlated with Si/Al ratio. High acidity is associated with higher aluminium content, above a Si/Al ratio of 7.

In addition to bridged hydroxyls in the channels, there are terminating silanol (Si-OH) groups at defect sites and at the surfaces of the zeolite crystals which arise where bonding would normally occur with adjacent T-atoms in the framework.

Lewis acid sites are believed to occur at high temperatures (>500^{o}C) by dehydration[20] (Figure 6).

Figure 6



The Lewis acidity may be attributed to the tricoordinated aluminium atoms, however, these sites are not well characterised. Alternatively, it may arise from non-framework aluminium, eg. AlO^+ species dislodged from the framework during pre-treatment or activation procedures. Lewis sites can also be introduced as the charge-compensating cations, e.g. Cu(II) exchanged zeolites can be reduced to Cu(I) with carbon monoxide.

Acidic zeolites are commonly prepared by ion-exchange with ammonium salts followed by thermal decomposition to dispel ammonia (Figure 7). Direct ion-exchange with protons from acidic solution is only feasible for high silica zeolites as dealumination and structural breakdown can occur. Where the zeolite is prepared in the presence of an organic cation, calcination in air leads to removal of the cation by oxidation and formation of Bronsted acid sites.

Acid sites are also generated in zeolites exchanged with bivalent or trivalent cations, followed by calcination. It is assumed that protons arise from dissociation of the water of hydration of the cation (Figure 8). Also, metal/acid bifunctional catalysts are formed by ion-exchange with transition metal ions, followed by reduction of the ion to the metal.

Figure 7

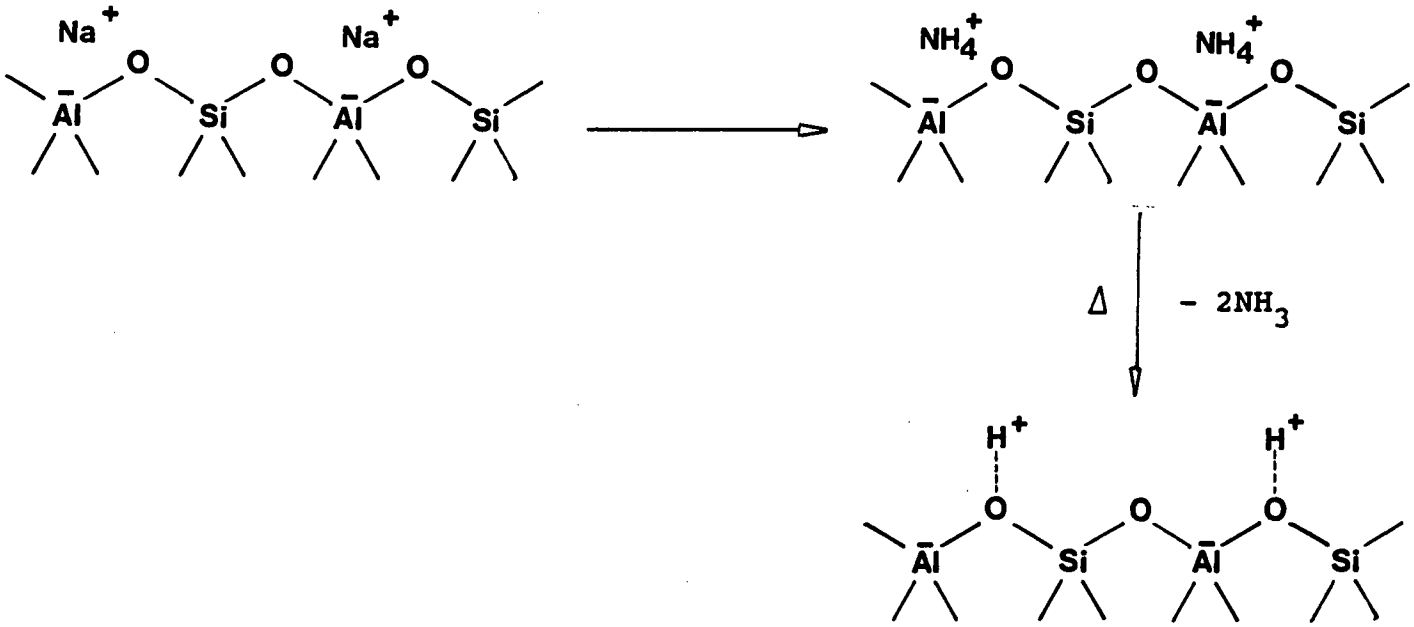
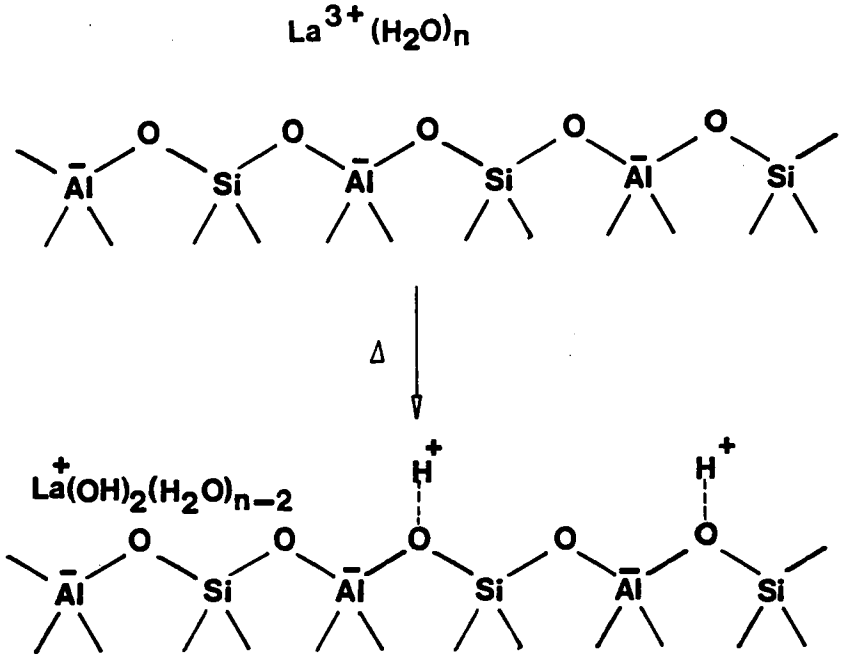


Figure 8



In addition to aluminosilicates, zeolite science has seen the development of materials with alternative T-atoms, e.g. frameworks where Al is replaced isomorphously by B, Fe, Cr or Ga and Si by Ge or Ti. These also have a net negative charge. The $AlPO_4$ [16,21] series of aluminophosphate molecular sieves have Al^{III} and P^{V} framework T-atoms in a 1:1 ratio and are thus neutral.

1.1 Application of zeolites to organic synthesis

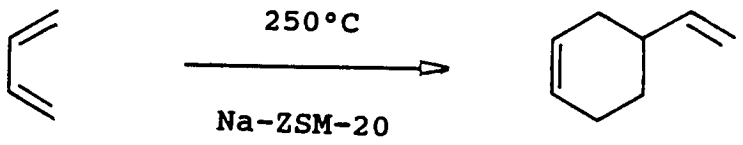
Zeolites are important catalysts in the oil and petrochemical industries because of their strong acidity and shape selectivity. The origin of this selectivity has been classified into three types[2] - reactant, product and transition state. Reactant selectivity is illustrated by the selective cracking of n-alkanes from a mixture of branched and n-alkanes; the branched alkanes are too bulky to diffuse into the pores. In the selective synthesis of <u>para</u>-xylene from toluene and methanol, both product and transition state selectivity operate. The <u>ortho</u>- and <u>meta</u>- isomers are thermodynamically favoured, but the <u>para</u>-isomer diffuses from the pores much more rapidly. The <u>ortho</u>- and <u>meta</u>- isomers are converted to <u>para</u> by equilibration. In addition, the competing reaction, disproportionation to toluene and trimethylbenzenes, is restricted as a large bimolecular transition state is involved. Other zeolite - catalysed industrial processes include Fluid Catalytic Cracking (FCC) and the methanol to gasoline (MTG)

process where the products are restricted to C_1-C_{10} hydrocarbons.

Early interest in zeolites as catalysts for organic reactions was reviewed by Venuto and Landis in 1968[22]. Since then, there have been significant advances in zeolite science with the synthesis of new materials, especially the development of the thermally stable, strongly acidic, high silica zeolites. Since the outset of this work there has been renewed interest in the application of zeolites to organic synthesis, as demonstrated by recent reviews. Comprehensive reviews by Hoelderich[23,24] make particular reference to potential industrial applications and van Bekkum[25] has examined the application of zeolites to the synthesis of fine chemicals. The majority of reactions are acid-catalysed and the range includes aromatic and aliphatic substitutions, isomerisations, rearrangements, addition and elimination, oxidation, condensation, oligomerisation and Diels-Alder reactions. The scope of the application of zeolites to organic synthesis is illustrated here.

Some examples employ the zeolite channels and cages although the zeolite plays no direct catalytic role. For instance, the Diels-Alder cyclodimerisation of buta-1,3-diene (1) to 4-vinylcyclohexene (2) is significantly enhanced in the presence of large-pore, non-acidic zeolites[26]. The effect is similar to the use of elevated pressures by the increased concentration of butadiene inside the zeolite pores relative to the external phase. The greater effectiveness of large-pore zeolites

compared to small-pore zeolites is attributed in part to the greater space available for the proper alignment of reactant molecules.



(1) (2)

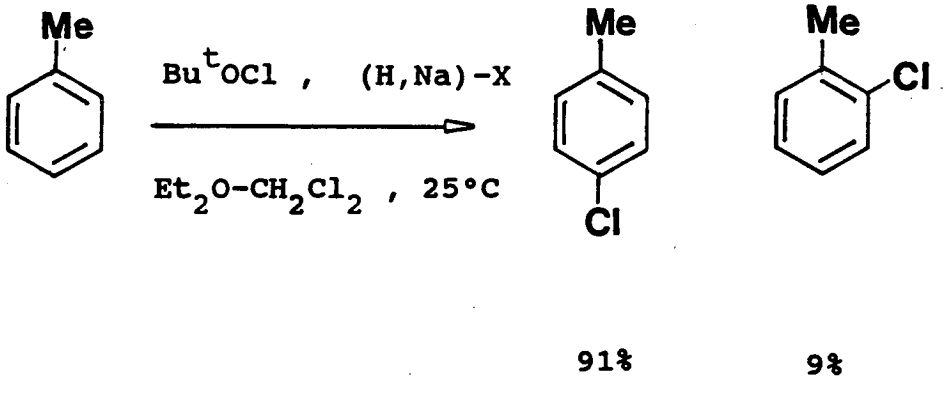
The Sharpless asymmetric epoxidation of allylic alcohols is reported to show enhanced conversion in the presence of 3A or 4A zeolites[27], an effect attributed to protection of the titanium isopropoxide catalyst from moisture. Zeolites have also been utilised as "cages" for photolytic reactions. For instance, altered product distributions were observed for the photolysis of dibenzyl ketones absorbed into zeolites[28].

However, most of the reported applications of zeolites in organic synthesis are acid-catalysed, carbocation mediated reactions. For example, the halogenation of aromatics is usually performed with Lewis or mineral acid catalysts at 20-80 ^{o}C. The reaction is also catalysed by zeolites (Na,Ca)-X and (Na,Ca,Fe)-X in the liquid phase[29]. When sufficient catalyst was used to allow complete sorption of the reactants high <u>para/ortho</u> ratios were observed. Over various Y-type zeolites the bromination of halobenzenes proceeds readily at 25^{o}C to yield substantially higher <u>para/ortho</u> ratios than with

conventional catalysts[30]. Zeolites with high Bronsted acidity were most active, an observation attributed to activation of bromine by acidic hydroxyl groups. However, the para-selectivity declined as the reaction proceeded. It was concluded that the zeolite was deactivated by HBr evolved during the reaction. Removal of the HBr by the addition of sodium hydrogen carbonate and K-A zeolite substantially increased the para/ortho ratio. Recently, it was reported[31] that para-selectivity in the Na-Y catalysed bromination of toluene is further enhanced in the presence of propylene oxide as HBr scavenger. The product was para-bromotoluene of 98% purity.

In addition, partially proton-exchanged zeolite X (H,Na)-X catalyses the chlorination of toluene by tert-butyl hypochlorite and produces a marked increase in para-selectivity[32] (Scheme 1).

Scheme 1



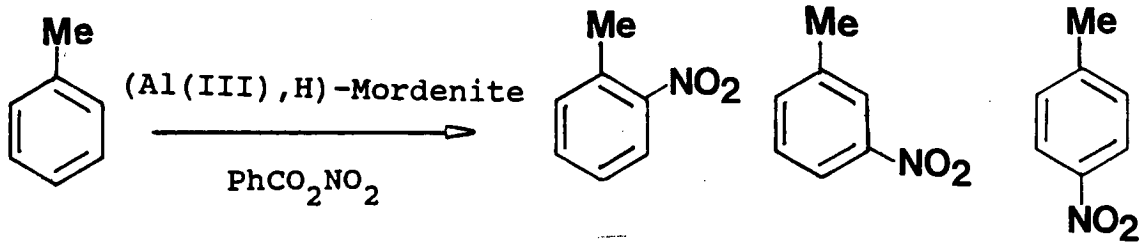
A series of alkyl and halobenzenes were examined as substrates. Enhanced para/ortho ratios were observed in each case, attributed to restriction of the ortho transition state within the channels. In contrast, using ZSM-5 zeolites as catalysts for the gas-phase chlorination of benzene at 175 ^{o}C, addition and not aromatic substitution was observed predominantly, to yield a mixture of hexachlorocyclohexane isomers[33].

It was concluded that materials with high Si/Al ratios favour homolytic dissociation of chlorine leading to a free-radical process, whereas materials which are more rich in alumina (or surface hydroxyl groups) favour an ionic process generating an electrophilic chlorine species. However, radical reactions on zeolites have been much less extensively examined than acid catalysed ones.

The para-selective nitration of aromatics has also been successfully achieved with zeolite catalysis.

Under common nitration conditions, with a mixture of sulphuric and nitric acids, a 2:1 ortho/para ratio is observed with toluene substrate. With an aluminium exchanged Mordenite zeolite and benzoyl nitrate, the para-isomer is formed predominantly in 67% yield[34] (Scheme 2).

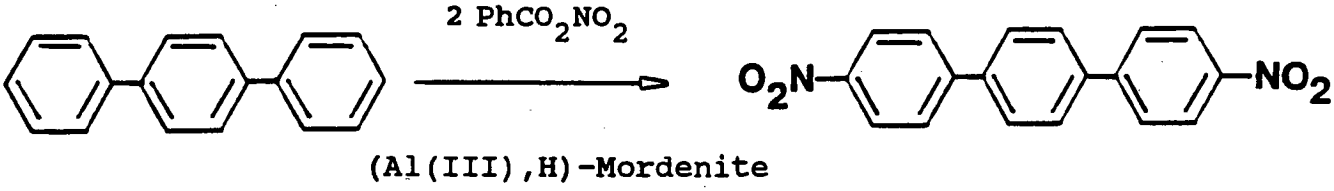
Scheme 2



32 : 1 : 67

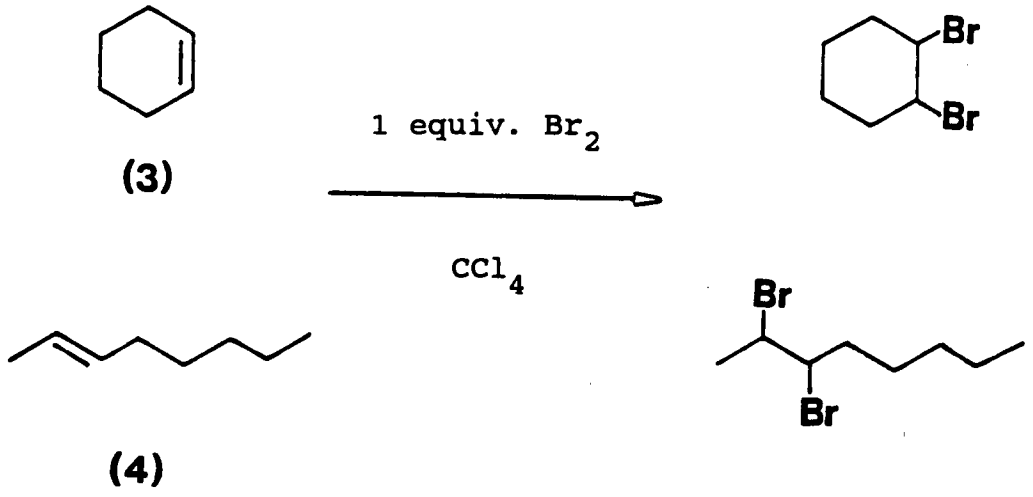
The process has also been applied to the synthesis of <u>para</u>, <u>pará</u>-dinitroterphenyl[34] (Scheme 3). It is claimed that the 71% yield obtained is the highest ever recorded for this reaction. Indeed, the size and shape of this molecule would seem to be ideally suited for zeolite-catalysed substitution reactions.

Scheme 3



The concept of shape-selectivity in zeolites is further highlighted by the liquid phase bromination[34] of an equimolar mixture of cyclohexene (3) and 2-octene (4) (Scheme 4).

Scheme 4

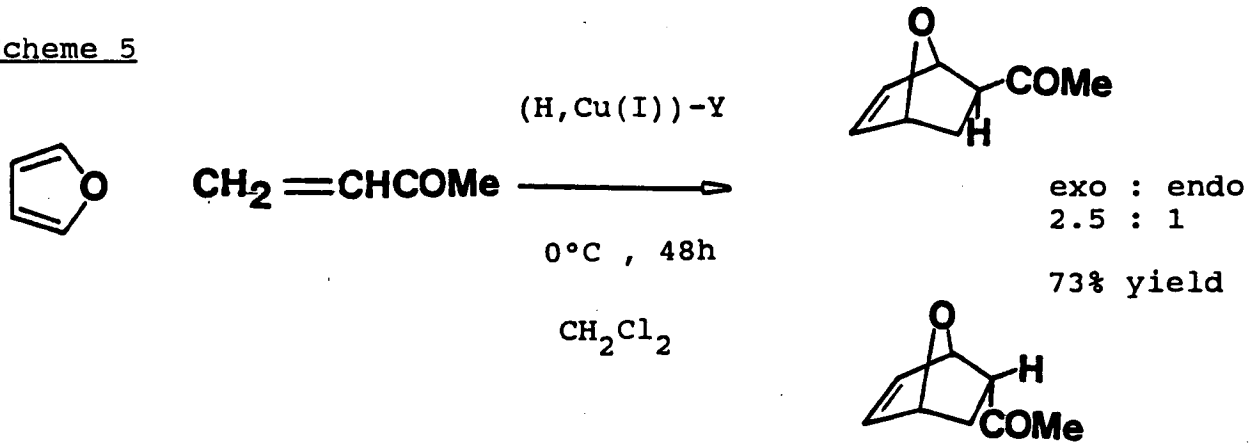


In the absence of zeolite, bromination of cyclohexene versus 2-octene was in the ratio of 60:40. When a zeolite was first added to the mixture and bromine added some minutes later, only the cyclohexene reacted. It was concluded that all the 2-octene was sorbed but the cyclohexene molecules were too large to diffuse into the pores. Conversely, when the bromine was added to the zeolite before the addition of the alkene mixture there was predominant reaction of the 2-octene. The zeolite and reaction conditions in this example were not disclosed.

Acid catalysed Diels-Alder reactions in the presence of zeolites have also been reported[35]. (H,Cu(I))-Y enhances the rate of cycloaddition and regio-selectivity of dienes such as furan and cyclopentadiene with a series of acrylic and

acetylenic dienophiles. The catalyst contains both Bronsted acid sites and Cu(I) ions as Lewis acid sites (Scheme 5).

Scheme 5



Another acidic zeolite-catalysed reaction is the Beckmann rearrangement of cyclohexanone oxime to ϵ-caprolactam[36] over H,Na-Y zeolites. A by-product, 5-cyanopent-1-ene, is formed mainly on the Na^+ ions. The process was performed in the gas phase at 355°C.

The performances of zeolites as bifunctional catalysts is demonstrated by the acid-catalysed aldol condensation of acetone over Pd-ZSM-5 in the presence of hydrogen at 180°C[37]. The reaction yields the hydrogenated product 4-methylpentan-2-one. However, neither the Beckmann rearrangement nor aldol condensation examples show significant selectivity.

Recent reports have demonstrated the application of zeolites for the synthesis of polymeric "molecular wires". Oxidative polymerisation of thiophene, 3-methylthiophene[38] and of pyrrole[39] occurs in zeolites Y and Mordenite exchanged with

Cu^{II} and Fe^{II} ions as oxidants. The "molecular wires" are stabilised within the channels.

Thus zeolites have potential in organic synthesis as shape-selective catalysts. Their activity can be selected by choice of cation and Si/Al ratio, and the channel size by choice of zeolite. These materials offer advantages over conventional catalysts in that they are catalytic in less than stoichiometric quantities, thus re-usable, and can be readily separated from the products.

Most reactions in this field which have been reported to date are gas phase[23,24]. The present work set out to examine liquid phase, acid-catalysed reactions where zeolites offer selectivity and potential application as common laboratory reagents.

2. THE CLAISEN REARRANGEMENT

2.1 Introduction

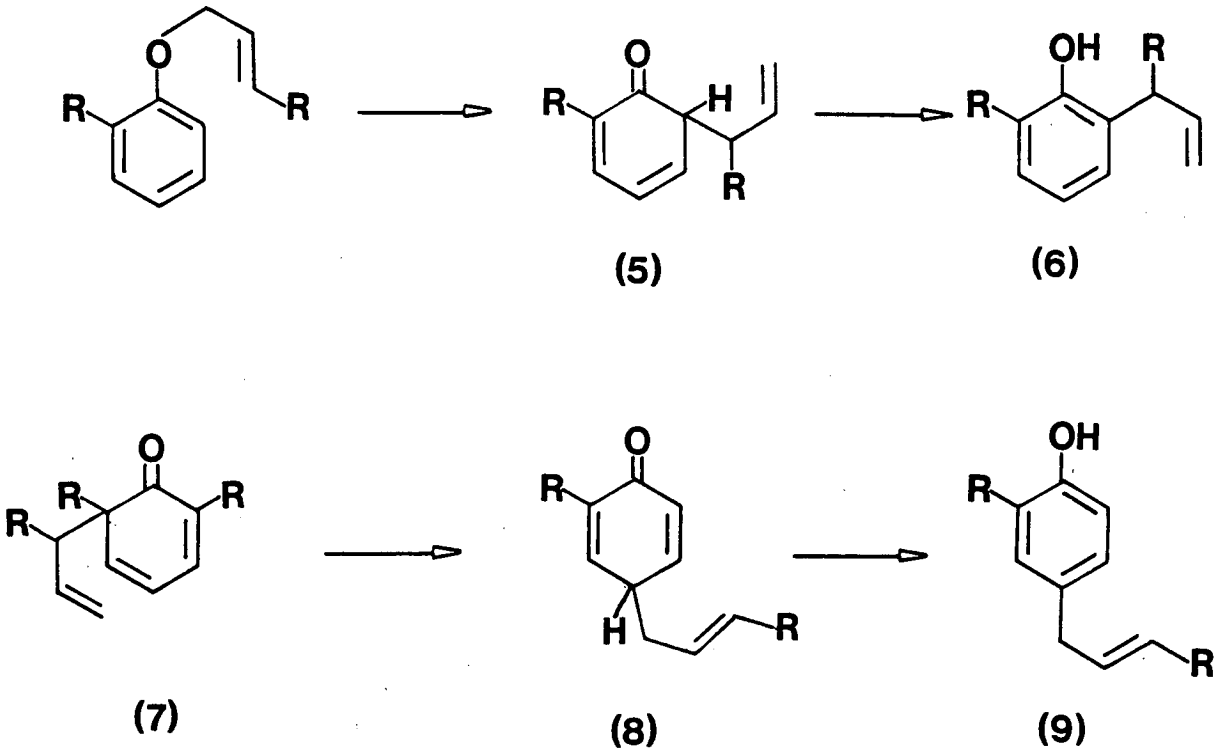
The thermally induced Claisen rearrangement[40-43] of allyl vinyl and allyl aryl ethers is considered to occur *via* a concerted pericyclic [3,3] sigmatropic shift as shown below.

The carbon analogue of the process is known as the Cope rearrangement. The reaction also occurs when the oxygen is replaced by heteroatoms such as sulphur or nitrogen, termed the thia- or aza- Claisen rearrangement respectively. Thus, the process covers a range of substrates and has been widely utilised as a stereo- and regio-selective process in organic synthesis[44].

In the rearrangement of allyl aryl ethers, the aromatic ring serves as the vinyl group. The accepted mechanism (Scheme 6) for the thermal rearrangement of allyl aryl ethers proceeds by an initial [3,3] shift to an *ortho*-dienone (5). If the *ortho*-substituent is hydrogen, rapid enolisation may occur at this stage to yield an *ortho*-allylphenol (6). In this *ortho*-rearrangement, the migrating allyl group undergoes structural inversion. If the *ortho*-position bears a substituent other than hydrogen (7), enolisation cannot occur and a second [3,3]

step (a Cope rearrangement) takes place. Subsequent enolisation of the para-dienone (8) gives the para-allylphenol (9), in which the original structure of the allyl group is restored.

Scheme 6



Thus, if both ortho positions bear substituents, the para-rearrangement occurs exclusively. If the para-position is substituted and an ortho-position is open then only ortho-allylphenol is obtained. For thermal rearrangements in which an ortho-site is free, migration to this position is generally

favoured. However, there are a number of reactions in which mixed products are formed. For example, allyl phenyl ethers substituted in the 2-position by -Me,-Et, isopropyl or t-butyl yield both 4-allyl and 6-allyl products[45]. In exceptional cases, the para-rearrangement has been observed even when both ortho-positions are free, e.g. 3,5-disubstituted crotyl phenyl ethers have been reported to give a mixture of ortho- and para-products[46], probably because of steric repulsion between the substituents in the ortho-dienone transition state. Migration to the meta-position has not been observed in the thermal reaction.

2.1.1. Catalysis of the Claisen Rearrangement

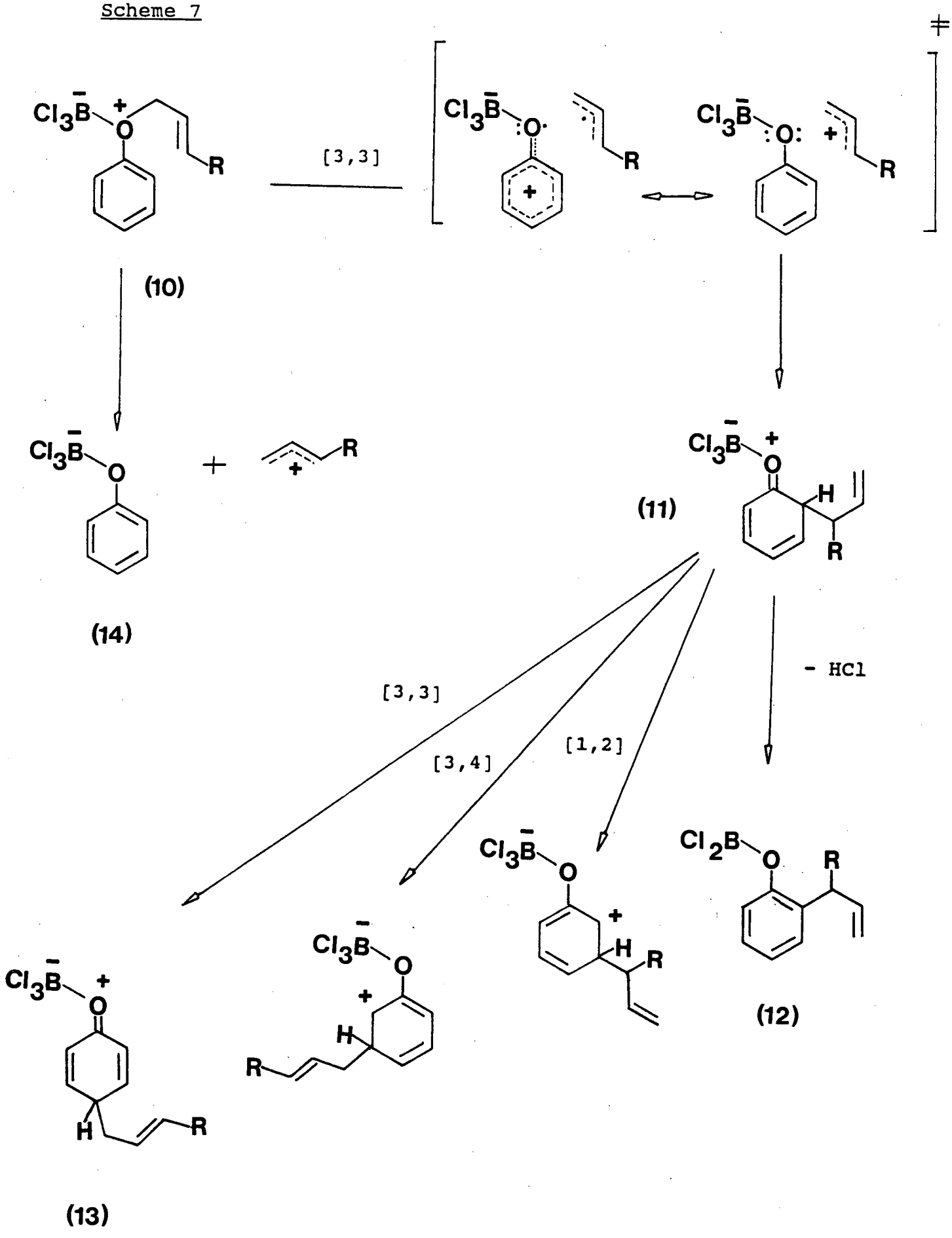
A number of catalysts have been reported for the Claisen rearrangement. These are mainly Lewis and Bronsted acids and transition metal complexes. As this area was comprehensively reviewed by Lutz[47] in 1984, only a summary of those catalysts which have been employed and the mechanisms proposed for the catalysed reactions are given here. Of particular interest to the present study was the Claisen rearrangement of allyl phenyl ether. Specific catalysts and reaction conditions which have been reported for this substrate are discussed in Section 2.3.

Of the Lewis acids which have been reported to promote the Claisen rearrangement, BCl_3 has been most extensively investigated. Schmid and co-workers[48,49] studied the BCl_3-promoted rearrangement of a number of allyl aryl ethers. As in

the thermal case, rearrangement to the ortho-position predominated when this site was free. A [3,3] sigmatropic mechanism has been shown to operate in these catalysed reactions. Inversion of the allyl group in the rearrangement of allyl phenyl ether to 2-allylphenol was demonstrated by ^{14}C labelling. This allylic shift was also observed in the rearrangement of allyl 2,6-dimethylphenyl ether to the para-product. Crossover experiments indicated that this process was intramolecular. Schmid and co-workers have proposed a charge-accelerated [3,3] sigmatropic rearrangement mechanism (Scheme 7). An initial BCl_3-ether complex (10) may undergo [3,3] rearrangement through a charge-delocalised transition state to the ortho-dienone intermediate (11). Loss of HCl would give the product complex (12). However, as in the thermal rearrangement, if the ortho- position is not substituted, a subsequent [3,3] rearrangement yields the para-product (13).

A number of side reactions were observed in some examples of the acid-catalysed process which do not occur in the thermal reaction. Allyl phenyl ethers with two ortho-substituents yielded meta-products as well as the expected para-products. Labelling experiments showed that these were formed via further [3,4] and [1,2] shifts from the ortho-dienone intermediate. Other products were cleavage phenols and ortho-allylphenols without structural inversion. For example, crotyl phenyl ether gave 28% cleavage phenol, 55% of the ortho allyl phenol with structural inversion, 4.5% of the ortho-allylphenol without inversion and 7.5% of para-allylphenol[49]. Therefore, the

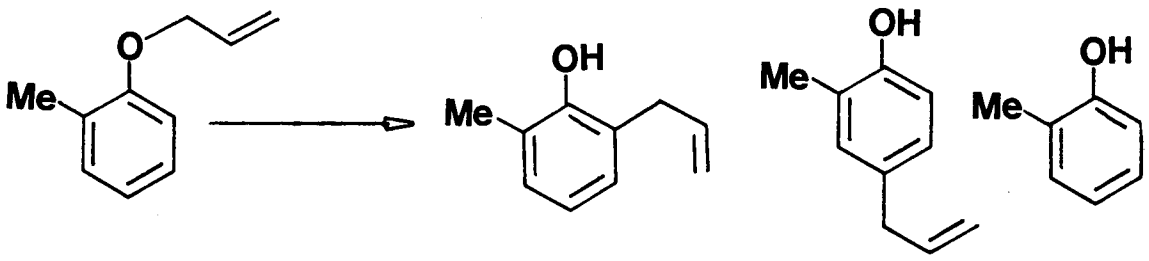
Scheme 7



scheme also includes cleavage of the ether - BCl_3 complex (14), which could lead to intermolecular processes.

A "para-effect" was observed in the catalysed reactions. Rearrangement of allyl aryl ethers with one alkyl group in the ortho-position gave both the ortho- and para-allylphenols, but more para-product was present than in the corresponding thermal rearrangement. This effect is attributed to the steric bulk of the BCl_3 complex and is illustrated in Table 2 for 2-methylallyl phenyl ether[49](15).

Table 2 Rearrangement of 2-methylallyl phenyl ether



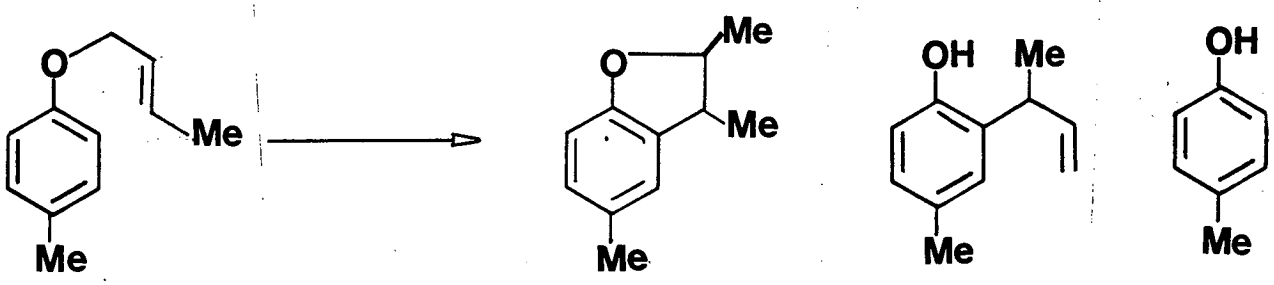
		(mol %)	
BCl_3	60	31.5	2
Thermal	80	15	-

Other examples of Lewis acid catalysis have been reported, but not systematically studied. These include BF_3 and BBr_3, which gave more side reactions than BCl_3, and Me_2BBr. Since 1984, $BF_3.OEt_2$ has been reported to promote the rearrangement of aryl

dienyl ethers[50] and of 4'-(1,1-dimethyl-alloxycoumarates)[51]. BCl_3 has also been observed as a catalyst for the rearrangement of 4'-allyloxycoumaric acid derivatives[52]. The review by Lutz[47], also covers examples of catalysis by alkylaluminium compounds, Grignard reagents, $SbCl_5$, $SnCl_4$, $ZnCl_2$ ([3,3] processes have been shown to operate with this catalyst), $TiCl_4$, $AgBF_4$, $AgCO_2CF_3$, $FeCl_3$ and $Hg(CF_3CO_2)_2$.

Bronsted acid catalysis of the Claisen rearrangement by CF_3CO_2H and H_2SO_4 has been demonstrated[53-55]. With both these catalysts, further acid-catalysed cyclisation of the ortho-allylphenol products to cyclic dihydrobenzofurans was observed, e.g. after 14.5 hours at room temperature, crotyl 4-methylphenyl ether in trifluoroacetic acid as solvent, gave 69% of 2,3-dihydro-2,3-dimethylbenzofuran, 8% of the ortho-allyl phenol and 8% cleavage phenol (Scheme 8).

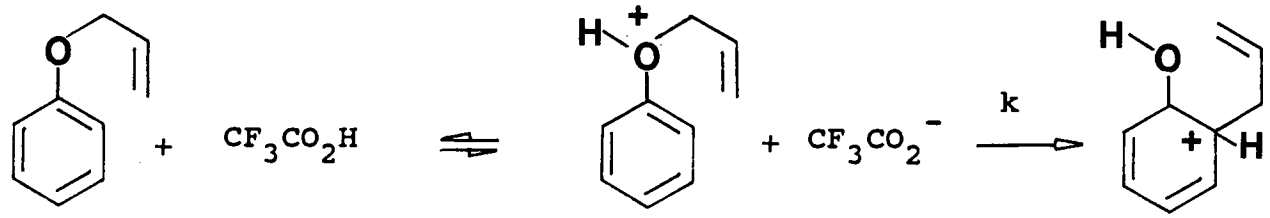
Scheme 8



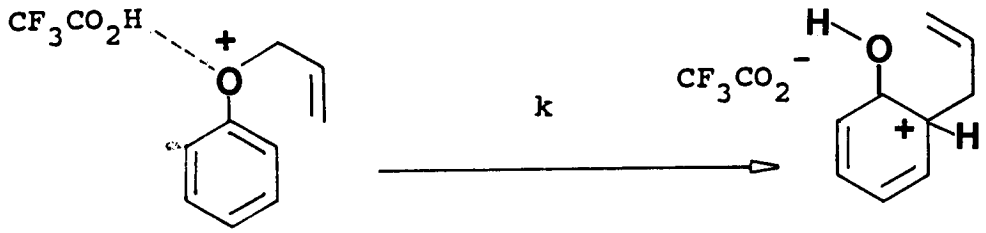
Schmid and co-workers[53] also considered these CF_3CO_2H- promoted reactions to be charge-accelerated [3,3] sigmatropic rearrangements. Svanholm and Parker[54,55] have suggested that CF_3CO_2H could be involved in two ways (Scheme 9). Protonation of the substrate may take place in a pre-equilibrium step, followed by rate-determining rearrangement (a), or by proton transfer from CF_3CO_2H concerted with rearrangement (b).

Scheme 9

(a)



(b)



In addition, there is a recent example of a base-catalysed[56] aromatic Claisen rearrangement of 3-hydroxyallyl phenyl ethers by aqueous methanolic potassium hydroxide in the presence of oxygen. To date, there have been no reports of zeolite-promoted Claisen rearrangements.

2.1.2 Rearrangement of allyl phenyl ether

In the present study the Claisen rearrangement of allyl phenyl ether [APE, (16)] in the presence of various zeolites was investigated. For comparison, the products and reaction

conditions of thermal and catalysed rearrangements are discussed in this section.

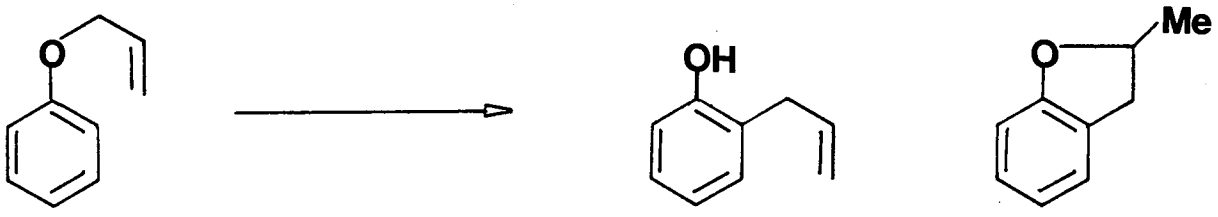
Thermal rearrangement of APE (16) gives high yields of 2-allylphenol [2-AP (17)] and a small amount of 2-methyldihydrobenzofuran [DBF (18)].

Thermal rearrangements in the literature where the yields were reported are shown in Table 3. It can be seen that the reaction is normally performed in the absence of solvent at reflux temperature (190-220^{o}C) for 5-6 hours.

Table 3 Thermal rearrangement of allyl phenyl ether

	conditions	2-AP yield (mol %)	DBF	ref
1.	reflux, 5-6h, neat	73	"small amount"	57
2.	reflux, 6h, neat	80	4-6 max	58
3.	pyrolysis, CO_2 atm., neat	90	a	59
4.	reflux, 5.5h, neat	42	4	60
5.	reflux, 6h, neat	77	a	61

a - not reported



(16) (17) (18)

There have been no reports of 4-allylphenol (4-AP) as a product in the thermal rearrangement of APE. It was not observed even in a specific attempt to detect it in pyrolysis products[62]. The low yield in entry 4 of Table 3 was attributed to polymerisation of the 2-AP product.

The Claisen rearrangement of APE has been catalysed by BCl_3[63] (Table 4). Greater than molar equivalents of BCl_3 were employed. The cyclic material, DBF, was not reported as a product but at 0°C both 4-AP and diallylphenols were observed.

Table 4 Claisen rearrangements of APE catalysed by BCl_3

conditions	time (min)	2-AP	4-AP	phenol	2,6 diallyl phenol	2,4 diallyl phenol	tot
		mol % products [a]					
0°C, neat	22	50.5	2.1	>4.6	6.4	10.5	>74.1
10°C, 20xPhCl	15	82.5	-[b]	0.2	0.2		83.0
10°C, 40xPhCl	23	90.8	-[b]	-[b]	-[b]		90.8

a - determined by g.c.
b - no other products detected

A number of alkylaluminium compounds also promote rearrangement of APE[64]. These reactions were performed in hexane with a 2:1 molar ratio of the alkylaluminium to APE (Table 5).

At room temperature, in methylene chloride as solvent, $TiCl_4$ yielded 88% of 2-AP[65] when two molar equivalents of catalyst were employed. $ZnCl_2$[66], MeMgI[67] and $AlBr_3$[68] also catalyse the rearrangement but yields were not reported.

In addition, proton acid catalysis by CF_3CO_2H gave the yields shown in Table 6, utilising a 0.5M solution of APE in CF_3CO_2H at 60°C[53]. It can be observed that increased reaction time leads to greater quantities of DBF *via* cyclisation of 2-AP.

Table 5 Rearrangement of APE catalysed by alkylaluminium compounds[64]

Alkylaluminium[a]	2-AP	DBF
	mol %	
Et_2AlCl	92.7	-[b]
$Et_2AlCl.Cl_2AlEt$	89.8	2.9
$EtAlCl_2$	68.1	18.2
$(Bu^i)_2AlCl$	95.8	-[b]

a - conditions:- 30 min, room temp.
b - not detected

Table 6 Rearrangement of APE catalysed by CF_3CO_2H

time (min)	APE	2-AP	DBF	phenol	other prods.	total yield
	% distribution[a]					
26	60.1	35.7	3.1	1.1	-[b]	83.1
104	7.2	33.8	52.5	5.1	1.4	75.6
208	-[b]	13.3	75.7	9.8	1.2	77.9

a - determined by g.c.
b - not detected

The high yields of DBF in these acid-catalysed rearrangements are not unexpected, as 2-AP has been reported to cyclise under acid conditions to this product[59]. In each of these reactions, greater than stoichiometric quantities of catalyst were employed. Only in one instance was 4-AP observed. A 2% yield was reported from the rearrangement of APE with BCl_3 at 0^oC in the absence of solvent (Table 4). It was considered that zeolites might also promote the Claisen rearrangement and that steric restrictions within the zeolite channels might lead to enhanced yields of the para-product, 4-AP.

2.2 Results and Discussion

The Claisen rearrangement of allyl phenyl ether [APE,(16)] has been investigated in the presence of a range of zeolites, the structure and acidity of which were discussed previously (Section 1.1). Reactions were performed in the liquid phase by stirring APE with the catalyst in a 5:1 w/w ratio for 48h and

subsequent removal of the zeolite from product mixtures by centrifugation or filtration. In selected experiments, the rearrangement was monitored as a function of time to follow the formation of products. Temperatures of 100°C and 140°C were employed in the present study, in comparison to 190-220°C described previously for the thermal rearrangement (2.1.2). Product yields based on starting material (APE) were determined by h.p.l.c. and g.c. analysis. In addition, the presence or absence of components in the product mixtures was confirmed by ^{13}C n.m.r. spectroscopy.

At 100°C, the thermal, uncatalysed Claisen rearrangement of APE yielded only 2-AP (4%) after 48h. At 140°C, 2-AP (9%) and DBF (3%) were obtained (Table 7). As the reaction is known to be promoted by Lewis and Bronsted acids, acidic zeolites were examined as possible catalysts. H-Nu-2 and H-EU-1 gave enhanced yields of 2-AP, together with the cyclic product DBF (Table 7). It is concluded that these acid zeolites promote the Claisen rearrangement of APE. Furthermore, the para-substituted product 4-AP was detected in the H-Nu-2 systems. The results over H-Nu-2 at 100°C are also exhibited graphically to illustrate the conversion of APE to products (Figure 9). The decline in % APE with time and the build-up of 2-AP, 4-AP and DBF can be clearly seen. The yield of 2-AP reached a maximum after 8h. As 2-AP is known to cyclise to DBF under acidic conditions[59], the continued production of DBF up to 48h can be attributed to this process.

Table 7 Rearrangement of allyl phenyl ether over acid zeolites

catalyst	Si/Al	T (^{o}C)	time (h)	2-AP	4-AP	DBF	ph	APE	total
				(mol%)					
H-Nu-2[a,b]	13.2	100	1	23.6	1.6	3.2	7.3	61.4	97.1
			4	33.4	2.2	7.6	6.9	48.7	98.8
			8	35.8	2.2	8.2	6.6	42.2	95.0
			24	33.5	2.1	17.4	7.2	30.0	90.2
			48	31.4	2.2	25.0	8.0	22.2	88.1
H-Nu-2[a]	13.2	140	48	29.5	<0.5	33.3	5.2	11.0	79.0
H-EU-1[a]	21.9	100	4	5.2	-	-	1.6	92.6	99.4
			8	12.1	-	<0.5	3.9	85.0	101.0
			24	21.4	-	1.6	3.8	71.8	98.6
			48	24.9	-	2.9	4.2	66.6	98.6
H-Nu-10	54.4	100	1	<0.5	-	-	1.7	95.0	96.7
			4	<0.5	-	-	2.2	95.5	97.7
			8	1.0	-	-	2.2	93.7	96.9
			24	3.1	-	-	2.4	91.6	97.1
			48	4.2	-	-	2.6	84.9	91.7
None	-	100	48	3.8	-	-	4.2	92.5	100.5
None	-	140	48	8.6	-	2.7	6.5	73.9	91.7

- = not detected
a = presence of components confirmed by ^{13}C n.m.r.
b = these results also displayed graphically in Fig.9

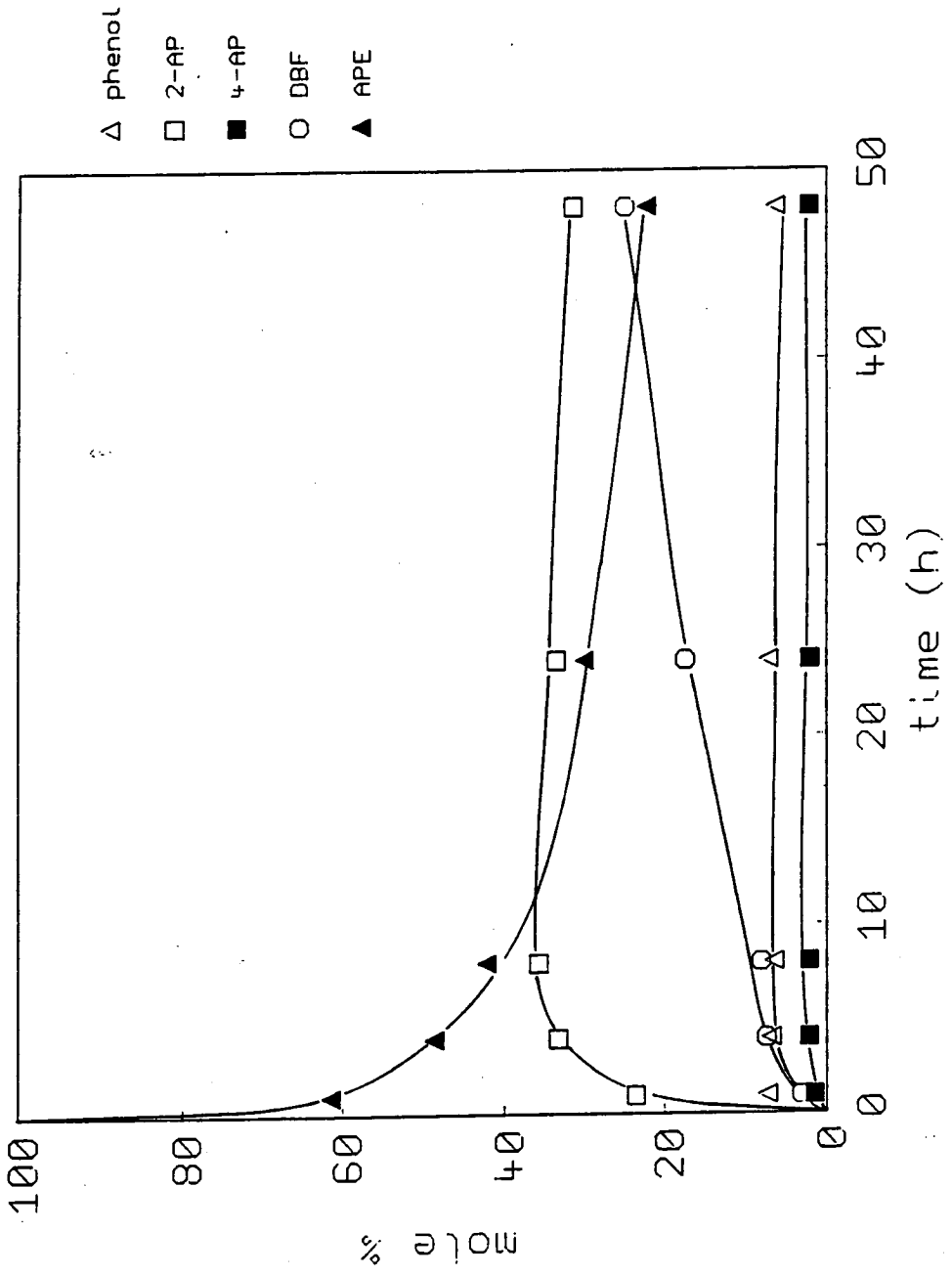


Figure 9 Claisen rearrangement of APE over H-Nu-2 at 100°C.

Over H-Nu-10 (Table 7), the products were similar to those of the thermal reaction which suggested initially that the narrower channels restricted sorption of APE and therefore subsequent rearrangement.

The catalytic effect of a range of H-Z5M-5 zeolites was also examined. As zeolite acidity can be related to the aluminium content (Section 1), four samples were synthesised with Si/Al ratios of 42.8, 64.3, 74.5 and 115.0 (Section 6.2.3). At 100^{o}C, after 48h, SKH-Z2 (Si/Al = 42.8) gave the greatest conversion to products (Table 8). This material had the lowest Si/Al ratio and therefore the highest aluminium content. Over SKH-Z4 (Si/Al = 115.0), the sample with the lowest aluminium content, there was little enhancement compared to the thermal, uncatalysed reaction. SKH-Z1 and SKH-Z3 had similar Si/Al (64.3, 74.5) ratios and both gave improved yields of 2-AP and DBF, comparable within experimental error. It should be noted however, that none of the above H-ZSM-5 samples produced yields as high as those observed with H-Nu-2 and H-EU-1.

Taking into account all of the acid zeolites represented in Tables 7 and 8, a plot of Si/Al ratio versus % conversion of APE after 48h at 100^{o}C indicates a general trend (Figure 10). Higher conversions of APE correspond to low Si/Al ratios. The Claisen rearrangement of APE is therefore promoted by acid zeolites, the extent of conversion being directly influenced by the aluminium content and thus, the acidity of the zeolite. The results for H-Nu-10 (Table 7) also fit into this

Table 8 Rearrangement of allyl phenyl ether over H-ZSM-5 zeolites

catalyst	Si/Al	T (°C)	time (h)	2-AP	4-AP	DBF	ph	APE	total
				(mol%)					
SKH-Z2	42.8	100	1	-	-	-	0.7	93.7	94.4
			8	4.0	-	<0.5	1.2	87.5	92.7
			24	11.8	-	0.7	1.9	79.8	94.2
			48	16.2	-	3.1	2.5	71.5	93.3
SKH-Z2[a]	42.8	140	48	35.0	-	12.2	4.5	44.8	96.5
SKH-Z1	64.3	100	1	-	-	-	0.7	98.9	99.6
			4	1.2	-	-	1.4	97.1	99.7
			8	4.1	-	-	1.4	94.3	99.8
			24	7.4	-	-	1.7	89.8	98.9
			48	12.7	-	0.7	2.0	84.8	100.2
SKH-Z3	74.5	100	1	-	-	-	1.1	96.4	97.5
			4	2.6	-	-	1.2	93.7	97.5
			8	4.0	-	-	1.5	91.1	96.6
			24	9.2	-	<0.5	1.9	86.6	97.7
			48	13.4	-	1.2	2.1	81.2	97.9
SKH-Z4	115.0	100	1	-	-	-	1.3	92.8	94.1
			4	-	-	-	2.3	90.6	92.9
			8	-	-	-	1.1	93.0	94.1
			24	2.7	-	-	1.6	89.9	94.2
			48	4.3	-	<0.5	1.6	88.3	94.2

- = not detected
a = presence of components confirmed by ^{13}C n.m.r.

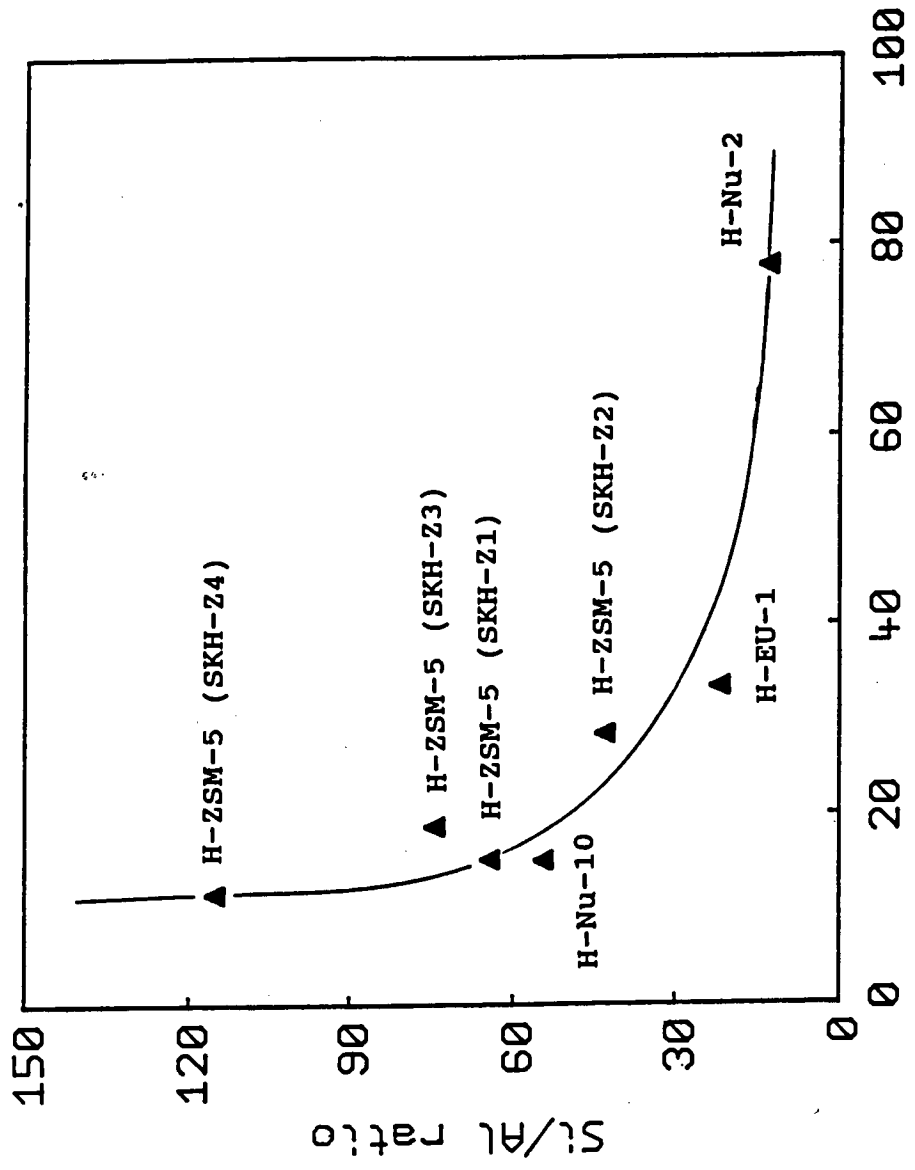


Figure 10 Si/Al ratio versus % conversion of APE after 48h at 100 °C.

relationship. Thus, APE might after all, be sorbed into the H-Nu-10 channels and the poor conversion in this case could be attributed to the relatively high Si/Al ratio. Of those acid zeolites studied, the greatest yield of DBF was observed in the presence of H-Nu-2. The low Si/Al ratio (Table 7) and thus high acidity of this material would lead initially to a high yield of 2-AP, followed by acid-promoted cyclisation to DBF.

A similar experiment at 100^{o}C over Nafion-H afforded a resinous product. Nafion-H is a polymeric, perfluorinated sulphonic acid resin which has found considerable use as a solid, superacid catalyst in organic synthesis[69]. After 1h, the product mixture was still mobile and g.c. analysis indicated that it contained 2-AP (3%) and APE (70%). However, after 4h, only phenol (7%) and DBF (6%) were detected. Similarly, after 48h, phenol (8%) and DBF (6%) were again the only products observed. 2-AP and APE were not detected and the remainder was attributed to higher boiling material which was not eluted from the column. Cationic polymerisation of both APE and 2-AP has previously been reported under strongly acidic conditions[70-71]. A similar process is feasible in this case, either of APE directly, or by initial rearrangement to 2-AP, followed by polymerisation. In addition, the low product accountability over H-Nu-2 at 140^{o}C (79.0%) might also be due to polymerisation. Nafion-H exhibits acidic character comparable to 100% sulphuric acid[69]. H-Nu-2 is unlikely to be as strongly acidic but it does have the lowest Si/Al ratio of all the zeolites studied.

Claisen rearrangement of APE over (Na,H)-Nu-10 (WZ 285) and (Na,H)-EU-1 was also investigated (Table 9). As well as Na^+ ions, these zeolites also contain some acidic sites. The protons are derived from the organic salts which are present throughout the synthesis. Compared to the thermal reaction, there was little enhancement over (Na,H)-Nu-10 at 140°C. In the presence of Na,H-EU-1, the yields of 2-AP (47%) and DBF (13%) were significantly improved, but 4-AP was not detected. The progress of this reaction was also monitored with time (Figure 11). As with H-Nu-2, maximum conversion to 2-AP was achieved after approximately 8h, but DBF was formed less rapidly and in lower yield.

The Na, Al and Si contents of the zeolites employed in the present work were determined by atomic absorption spectroscopy (Section 6.2) from which Si/Al ratios were calculated. The % Na content, i.e. the molar equivalents of Na relative to Al gives a measure of the remaining Al available for acid sites (Table 10). Thus, of the available aluminium sites in (Na,H)-EU-1, 13.5% are associated with Na^+ ions and the remainder (86.5%) are assumed to be associated with acidic sites. Compared to (Na,H)-Nu-10 (WZ 285), (Na,H)-EU-1 has a lower Si/Al ratio, thus more aluminium sites, a higher proportion of which are acidic sites. This rationale explains why the conversion of APE to Claisen rearrangement products is significantly greater over (Na,H)-EU-1 than (Na,H)-Nu-10, as

Table 9 Rearrangement of allyl phenyl ether

catalyst	T (^{o}C)	time (h)	2-AP	4-AP	DBF	ph	APE	total
			(mol%)					
(Na,H)-Nu-10[a]	140	1	<0.5	-	-	2.7	89.6	92.3
(WZ 285)		4	3.9	-	-	1.9	86.7	92.5
		8	7.0	-	-	1.7	82.5	91.2
		24	11.5	-	-	2.4	80.1	94.0
		48	14.3	-	1.3	3.3	72.0	90.9
(Na,H)-EU-1[b]	140	1	32.5	-	3.6	3.6	57.4	97.1
		4	44.8	-	9.0	5.2	39.2	98.2
		8	45.3	-	9.4	6.2	35.3	96.2
		24	44.8	-	10.0	5.6	30.8	91.2
		48	46.6	-	13.4	4.8	27.0	91.8
(Cu(II),H)-Y[a]	140	1	2.2	1.8	-	4.6	87.0	95.6
		4	6.5	4.9	<0.5	15.6	70.5	97.5
		8	11.2	8.7	<0.5	20.7	58.6	99.2
		48	22.0	5.7	1.1	18.9	43.1	89.7
(Cu(II),H)-Y	100	1	-	-	-	1.1	97.8	98.9
		4	-	-	-	1.8	94.6	96.4
		8	1.2	-	-	2.8	92.4	96.4
		24	4.7	1.0	-	5.8	85.5	97.0
		48	4.3	0.8	<0.5	5.0	88.7	98.8
None	100	48	3.8	-	-	4.2	92.5	100.5
None	140	48	8.6	-	2.7	6.5	73.9	91.7

a = presence of components confirmed by ^{13}C n.m.r.
b = these results displayed graphically in Fig.11
- = not detected

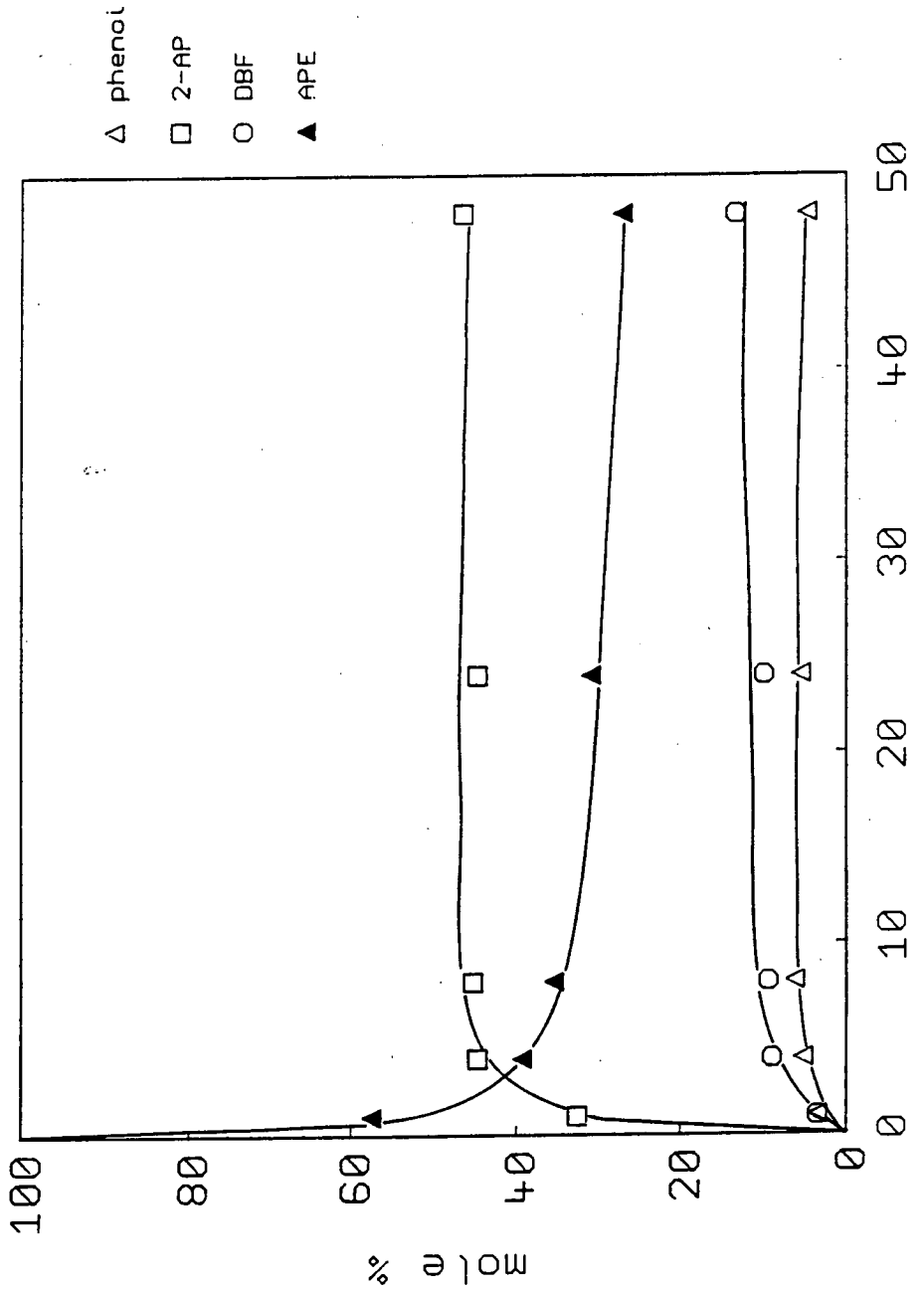


Figure 11 Claisen rearrangement of APE over (Na,H)-EU-1 at 140 °C.

the zeolite structures and channel dimensions are very similar (Section 1.1, Table 1).

Table 10 Relative Acidity of Zeolites

	% molar equivalents			
zeolite	% Na	H	Cu	Si/Al
(Na,H)-Nu-10 (WZ 285)	75.2	24.8	-	43.6
(Na,H)-EU-1	13.5	86.5	-	20.9
H-Nu-2	<0.1	>99.9	-	13.2
(Cu(II),H)-Y	16.4	23.4	60.2	3.0
(Na,H)-Nu-10 (AA53)	14.5	85.5	-	60.0

To confirm that DBF could be formed by cyclisation of 2-AP in the presence of (Na,H)-EU-1, a check experiment was performed. 2-AP and (Na,H)-EU-1 were heated at 140^{o}C using a 5:1 w/w ratio in an identical procedure to that described previously. DBF was obtained in 19.5% yield compared with 7.1% in the absence of zeolite. From this result, it is unlikely that cyclisation of 2-AP to DBF is favoured because of the confines of zeolite channels, e.g. by setting up a suitable transition state for ring-closure. Indeed, there is little evidence to suggest that any shape-selective effect occurs in the examples discussed above. The results in Tables 7-9 correlate well with relative acidity.

Also shown in Table 9 are the yields from experiments at 100°C and 140°C over (Cu(II),H)-Y. This was prepared by ion-exchange of NH_4-Y with $CuSO_4$ solution to give a pale-blue powder. Of the available aluminium sites, 60.2% are associated with Cu(II) ions (Table 10). Thus both Bronsted (as protons) and Lewis (as Cu(II) ions) acid sites were present. In comparison to the thermal rearrangement at 140°C, there was good conversion to Claisen rearrangement products 2-AP and DBF. Significantly, 6% 4-AP was formed with this catalyst along with a high yield of phenol.

Further experiments were performed in the presence of Na-Y, Na-A and $AlPO_4$-5 aluminophosphate molecular sieve (Table 11). With Na-A there was no enhancement compared to the thermal rearrangement presumably because the pores are too small for sorption of APE molecules (Section 1.1, Table 1). However, APE should be readily sorbed into the larger channels of Na-Y and $AlPO_4$-5. The latter materials gave yields of 20% and 15% of 2-AP respectively at 140°C, compared to 9% in the absence of zeolite. The slight activity of $AlPO_4$-5 can be attributed to irregularities in the structure giving rise to a few acid sites[72]. The Na-Y was a commercial sample which was not expected to contain acid sites, although the actual composition has not been determined. As $AlPO_4$-5 and Na-Y are large-pore structures (Section 1.1, Table 1) it is unlikely that the observed enhancements are caused by steric constraints on APE within the channels.

Table 11 Rearrangement of allyl phenyl ether over non-acid molecular sieves

catalyst	T (^{o}C)	time (h)	2-AP	4-AP	DBF	ph	APE	total
			(mol%)					
Na-Y	140	1	<0.5	-	-	<0.5	96.3	96.6
		4	3.2	-	-	<0.5	94.0	97.5
		8	6.2	-	-	<0.5	91.5	98.1
		24	15.7	-	<0.5	0.8	81.2	97.7
		48	19.6	-	1.3	1.7	75.4	98.0
Na-A	140	1	-	-	-	1.3	98.1	99.4
		4	0.8	-	-	1.0	97.8	99.6
		8	1.6	-	-	1.6	92.0	95.2
		24	2.8	-	<0.5	2.6	79.3	84.7
		48	5.3	-	2.1	4.4	73.6	85.4
$AlPO_4$-5	140	1	<0.5	-	-	1.0	90.6	91.6
		4	1.1	-	-	0.7	89.4	91.2
		8	2.2	-	-	0.8	91.6	94.6
		24	4.4	-	-	2.3	84.6	91.3
		48	14.6	-	1.2	3.9	68.2	87.9
None	140	48	8.6	-	2.7	6.5	73.9	91.7

- not detected

Prior to the above study, some initial investigations into the Claisen rearrangement were performed by sorption of APE into zeolites in a 1:3 w/w ratio. The APE was dissolved in methylene chloride, a known weight of zeolite was stirred into the solution and the solvent removed under vacuum. However, this method proved to be unsatisfactory, as low and inconsistent yields were obtained. The poor recovery was attributed to loss of APE under vacuum and evaporataion from zeolite during reaction exacerbated by the small quantities employed. While quantitative yields were not determined in most cases the experiments did confirm an improved production of 2-AP over Na-Y and the lack of enhancement over Na-A. An interesting comparison with the stirred reaction was observed over (Na,H)-Nu-10. A different batch of (Na,H)-Nu-10 was utilised (AA53) and after 5h at 140^{o}C the products were 2-AP (26.6%), DBF (17.2%), APE (1.1%) and phenol (0.2%), based on starting APE. Despite the low accountability, it is clear that the yields are increased relative to both the thermal reaction and the stirred system over WZ 285 (Table 9). A number of factors might contribute to this observation. While the composition of AA53 (Table 10) incorporates less Na than WZ 285, the Si/Al ratio is higher, so it would appear that the different effect is not only one of acidity. The ratio of zeolite to APE was 15 times greater (w/w) than in the stirred reaction. Also, the pre-sorption technique employed may lead to improved uptake of APE into the Nu-10 channels.

Table 12 shows the water uptake determined by thermal gravimetric analysis (t.g.a.) for these zeolites after equilibration in air. From the water sorption capacity, the quantity of APE sorbed into the channels can be estimated. The stirred reactions were performed with a 5:1 w/w ratio of APE to zeolite. For 1g of H-Nu-2, conversion of only 0.134g of APE would be expected. The total product yield was 65%. As considerably more APE was converted than can be sorbed by the zeolite, it can be concluded that these reactions are catalytic.

Table 12 Water uptake determined by t.g.a.

zeolite	wt. loss (%)	Si/Al
(Cu(II),H)-Y	25.7	3.0
H-Nu-2	13.4	13.2
(Na,H)-EU-1	9.3	20.9

To summarise, the Claisen rearrangement of APE can be catalysed by zeolites. The most effective materials were H-Nu-2, (Cu(II),H)-Y, (Na,H)-Eu-1 and H-EU-1. The most important factor for conversion is zeolite acidity, a measure of which can be obtained from the Si/Al ratio.

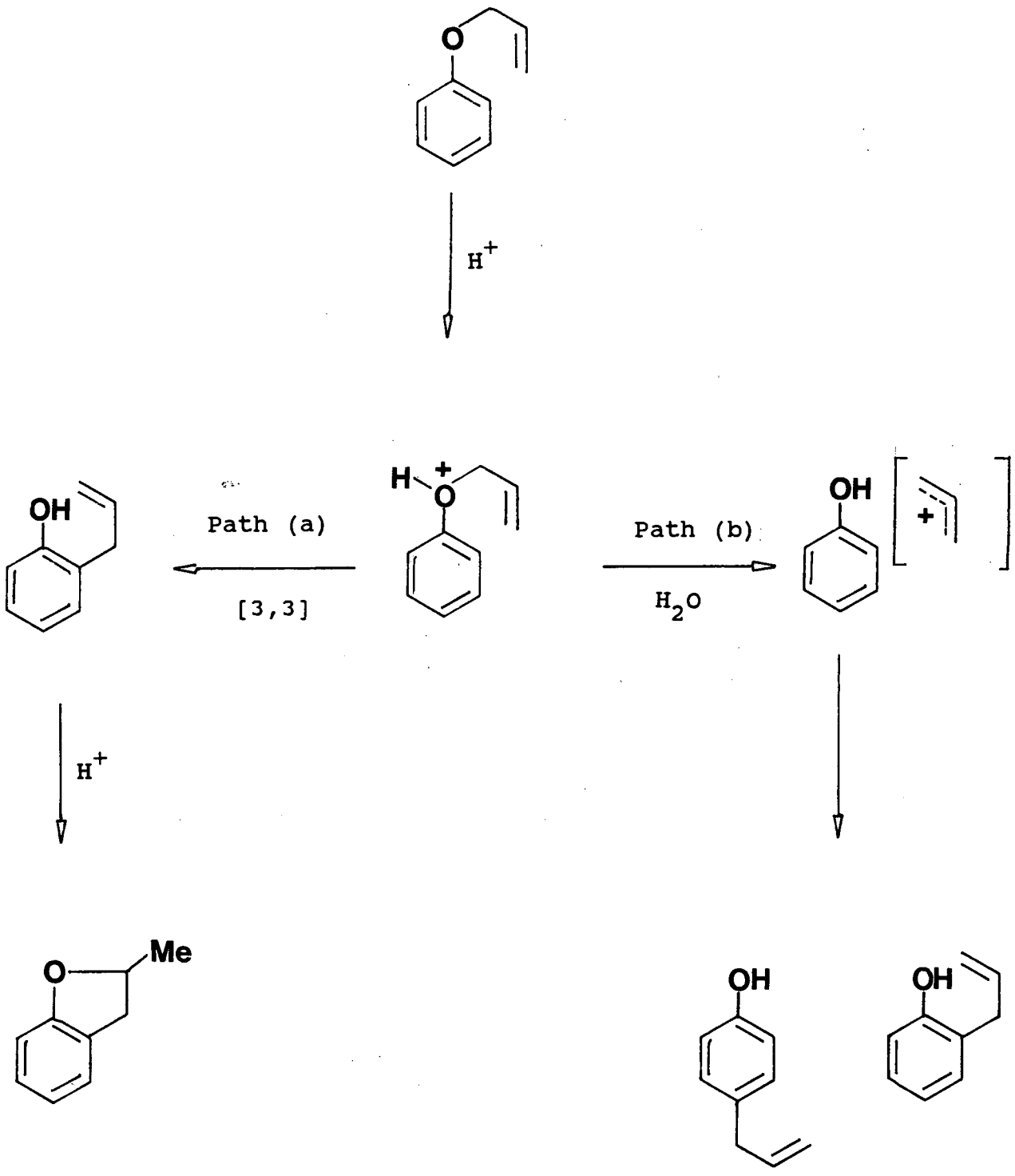
A significant by-product in the presence of acid zeolites was DBF formed by cyclisation of 2-AP. From the literature (Section 2.1.2), 4-AP is not a product of the thermal,

uncatalysed section but has been observed in small quantities in the BCl_3-promoted rearrangement of APE. 4-AP was only detected in the presence of H-Nu-2 and (Cu(II),H)-Y and not with (Na,H)-EU-1 or H-EU-1 despite the high conversion in these instances. As the former are both large-pore zeolites (Section 1.1, Table 1) it is unlikely that 4-AP was formed because of steric hindrance of the ortho-positions within the zeolite channels. These two materials have in common high acidity and high water sorption capacity (Tables 10 and 12). Concomitant with 4-AP formation were high yields of phenol. This information is consistent with an intermolecular process for production of 4-AP via acid-catalysed aromatic substitution at the para-position [Scheme 10, path (b)]. The particularly high quantity of phenol and 4-AP observed with (Cu(II),H)-Y can therefore be attributed to the high acidity and water uptake of the zeolite. Some of the catalytic activity in this case may arise from Cu(II) ions acting as Lewis acid sites. The large Cu(II) ions may also exert a steric effect and promote substitution at the para-position. In comparison to (Cu(II),H)-Y and H-Nu-2, EU-1 and ZSM-5 have a low water sorption capacity and aluminium content.

In the presence of zeolites, 2-AP was the major product, as in the thermal and BCl_3-catalysed rearrangement of APE. It could be produced by the intermolecular process depicted in Scheme 10 [path (b)] or by an intramolecular [3,3] shift [path (a)] similar to the charge-accelerated mechanism proposed by Schmidt et al (Scheme 7) for BCl_3.

Side products with BCl_3 catalysis were 2,6- and 2,4-diallyl phenol. These were not detected in significant quantities in the ^{13}C n.m.r. spectra of the products of the zeolite-catalysed reactions, presumably because a second allylic substitution would be prevented within the steric confines of the zeolite channels.

Scheme 10

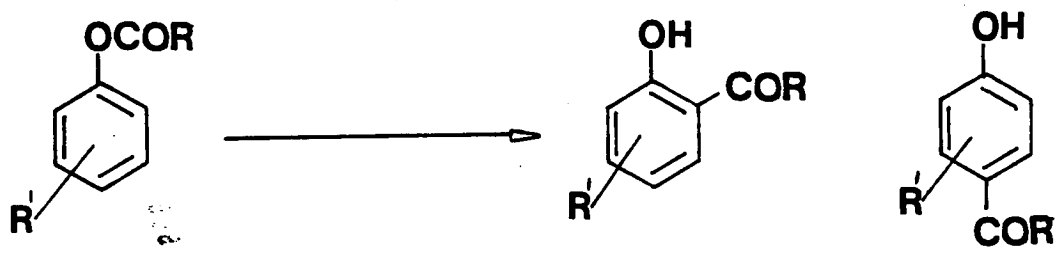


3. THE FRIES REARRANGEMENT

3.1 Introduction

3.1.1. General Background

The Fries rearrangement[73-76] is the conversion of a phenolic ester to ortho- and para-hydroxyphenyl ketones, or a mixture of both, in the presence of an acid catalyst. The corresponding meta-products are not formed, except where considerable steric factors operate.



Fries[77,78] observed the rearrangement of phenyl acetates and chloroacetates catalysed by aluminium chloride and recognised a general procedure for the synthesis of hydroxyphenyl ketones. Subsequently, the reaction has been extensively studied and shown to apply to a large number of esters. The wide scope has been covered in a number of comprehensive reviews.[73-76] A photo-Fries rearrangement, which does not require a catalyst has also been reported.[79-81]

A range of experimental conditions have been employed. Common solvents are nitrobenzene, tetrachloroethane, dichlorethane, carbon disulphide and light petroleum, but many reactions are readily performed in the absence of solvent.[74] Temperatures between 25°C and 180°C are usual and the reaction time can vary

between a few minutes and a few days. Although aluminium chloride has been most extensively used as a catalyst there are many alternatives. These are reviewed in Section 3.1.2.

The course of the rearrangement can be strongly influenced by experimental conditions. It has been reported that the proportion of para-isomer is increased in more polar solvents.[82] Yields of the ortho-isomer are generally greater in reactions performed at high temperatures than in the corresponding reactions at lower temperatures.[83-85] The para/ortho ratio is also known to be influenced by the relative ratio of the catalyst to the ester starting material.[85,86] Thus, comparisons between Fries rearrangements are strictly only valid between reactions performed under the same experimental conditions as a number of factors can influence the selectivity.

3.1.2. Catalysis

The Fries rearrangement is catalysed by both Lewis and Bronsted acids. Aluminium chloride has been most commonly used and is the usual choice for synthetic applications.[74] No rearrangement occurs in the absence of catalyst. For Lewis acids, an equimolar catalyst to ester ratio is required. Aluminium chloride decomposes during reaction with the evolution of hydrochloric acid. Therefore, Lewis acids are not catalytic in the rigorous sense as the active species is not regenerated.

In addition to aluminium chloride ($AlCl_3$), the following have been shown to be effective catalysts for the rearrangement of esters of naphthol and cresol:[87] $AlBr_3$, $HgCl_2$, $AlCl_3$-$HgCl_2$, $FeCl_3$, $CrCl_3$, $SnCl_4$ and $TiCl_4$. A comparative study on the influence of each acid on the yield and selectivity showed that $TiCl_4$, $AlBr_3$ and $AlCl_3$ were the most active but that the proportion of ortho and para products was influenced by the catalyst. With $TiCl_4$, the α-naphthoate ester gave a combined yield of 53% of ortho- and para- hydroxy products and was ortho-selective, whereas $AlCl_3$ gave a combined yield of 37% but was para-selective under the same reaction conditions.

The relative activity of catalysts for the Fries rearrangement has been studied by a number of other workers. $AlCl_3$, $SnCl_4$, $TiCl_4$ and $ZnCl_2$ catalyse the rearrangement of thymyl acetate, carvacryl acetate, m-ethylphenyl acetate and 3,5-dimethylphenyl acetate.[88] $ZnCl_2$ was the least active. For the conversion of furancarboxylic esters of halogenated and alkyl substituted phenols the order was found to be: $AlCl_3 > SnCl_4 > ZnCl_2$.[89] Catalyst activities for the rearrangement of phenyl caprylate[90] were $FeCl_3 > TiCl_4 > SnCl_2$, but with 4-acetoxycoumarin,[91] $FeCl_3$ was less efficient. The order was $TiCl_4 > AlBr_3 > AlCl_3 > SnCl_4 > FeCl_3 > CrCl_3$.

There are a number of other examples of catalysis by $TiCl_4$[92-97], $FeCl_3$[98], $AlBr_3$[86,99] and $ZnCl_2$.[100-102] Other effective Lewis acids include BF_3[102-105], $NbCl_5$[94], $TaCl_5$[94] and mixtures such as HCl-$ZnCl_2$[106], $AlCl_3$-NaCl[107,108] and HCl-$SnCl_4$.[109]

While the Fries rearrangement is traditionally performed with Lewis acids examples of Bronsted acid catalysis have been reported. HF[110-113], H_3PO_4[102], polyphosphoric acid[114-115], H_2SO_4[102], $NaHSO_4$[102], para-toluenesulphonic acid (p-$CH_3C_6H_4SO_3H$)[102,117], methanesulphonic acid (CH_3SO_3H)[102], methanetrisulphonic acid ($CH(SO_3H)_3$)[102] and trifluoromethane-sulphonic acid (CF_3SO_3H)[118,119] all promote the conversion to some extent. In some of these cases large quantities of catalyst were employed, similar to the rearrangements with Lewis acid. Conversion of phenyl benzoate has been achieved by dissolution of 15g in 150ml of neat, liquid HF[111]. In other examples, only catalytic amounts have been used. A 1:50 ratio of CF_3SO_3H[118] to phenyl benzoate gave good product yields.

Hocking[102] has compared a number of proton acids with the Lewis acids $AlCl_3$, BF_3 and $ZnCl_2$ as catalysts for the rearrangement of phenyl acetate. The Lewis acids were considered to give faster reaction. The proton acids were studied under a variety of conditions in terms of the catalyst to ester ratio, temperature and reaction time. Under the following conditions: 4h at 160°C, with a catalyst:ester ratio of 0.033, in the absence of solvent, methanesulphonic acid gave 2-hydroxyacetophenone (3%) and only a trace of the para-isomer, 4-hydroxyacetophenone. Other catalysts include p-$MeC_6H_4SO_3H$ (5% ortho, 0.7% para); $CH(SO_3H)_3$ (11%, 3%); H_2SO_4 (2%, 0.8%); H_3PO_4 (6%, 2%). Thus, these Bronsted acids are ortho-selective

under the above conditions, with methanetrisulphonic acid the most active.

Catalysis by acidic ion-exchange resins has also been reported. Sulphonated polystyrene resins[121-123] have proved to be both catalytic and re-usable.

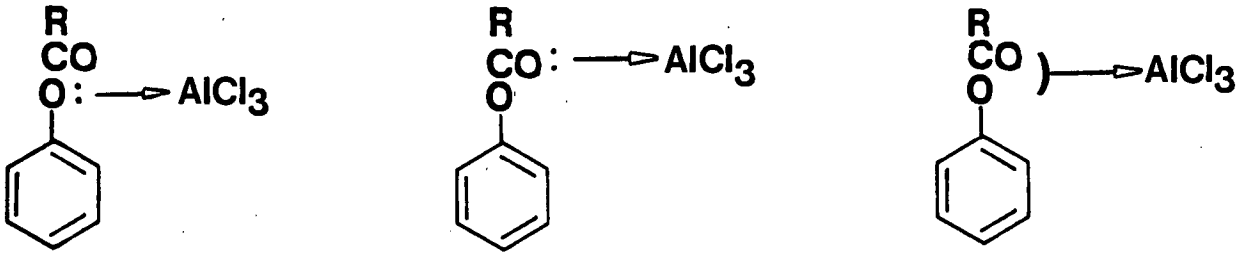
3.1.3. Mechanism

Despite much investigation, the mechanism of the Fries rearrangement is still not completely understood. There has been considerable debate as to whether it is an inter- or intra- molecular process. Some of the confusion has arisen because of the wide variety of reaction conditions employed by workers in this field. As the reaction can be strongly influenced by the experimental conditions any conclusions drawn for a specific rearrangement may not apply to another example unless the structures of the starting materials and conditions are similar. Most studies have been based on systems catalysed by aluminium chloride. The mechanism of rearrangements promoted by proton acids has not been investigated.

Three main pathways have been proposed. Evidence has been reported to support each, some of which is outlined in this section. None of these mechanisms has either been conclusively proved or rejected. It is generally accepted that the first step is the formation of a catalyst-ester complex.[73-76] This can be represented (Figure 12) with the catalyst coordinated to

either the phenolic (I) or carbonyl (II) oxygen of the ester group or the delocalised p-π electron system as a whole (III).

Figure 12



(I) (II) (III)

An intermolecular pathway via cleavage of the catalyst-ester complex to an intermediate acyl cation of acyl chloride and a phenol complex (Scheme 11) was first proposed by Skraup and Poller.[124] These moieties can react in a Friedel-Crafts type acylation to afford both the ortho- and para-hydroxyphenyl ketones.

This mechanism was supported by trapping experiments.[124] When rearrangement of m-tolyl acetate was attempted in the presence of m-chlorobenzoyl chloride, the benzoylation product of m-cresol was isolated instead of the Fries rearrangement products. It was concluded that m-cresol, formed by cleavage of the ester had undergone Friedel-Crafts acylation with the m-chlorobenzoyl chloride, expelling acetyl chloride from the reaction mixture. Collection and identification of acetyl chloride supported the conclusion that an intermolecular process had taken place.

Further evidence for an intermolecular mechanism came from competitive rearrangements of tolyl esters.[125] In the presence of diphenyl ether, an acyl group acceptor, both the hydroxyketone rearrangement products and 4-acetyldiphenyl ether were obtained. More recent investigators have also supported the acyl cation as an intermediate in the Fries rearrangement.[93,126,127]

Rosenmund and Schnurr[83] were also of the opinion that the rearrangement was intermolecular, but proposed a bimolecular pathway in which one molecule of the ester is acylated by another (Scheme 12). In crossover experiments with mixtures of two different esters, crossover products were observed in addition to the expected rearrangement products (Scheme 13).

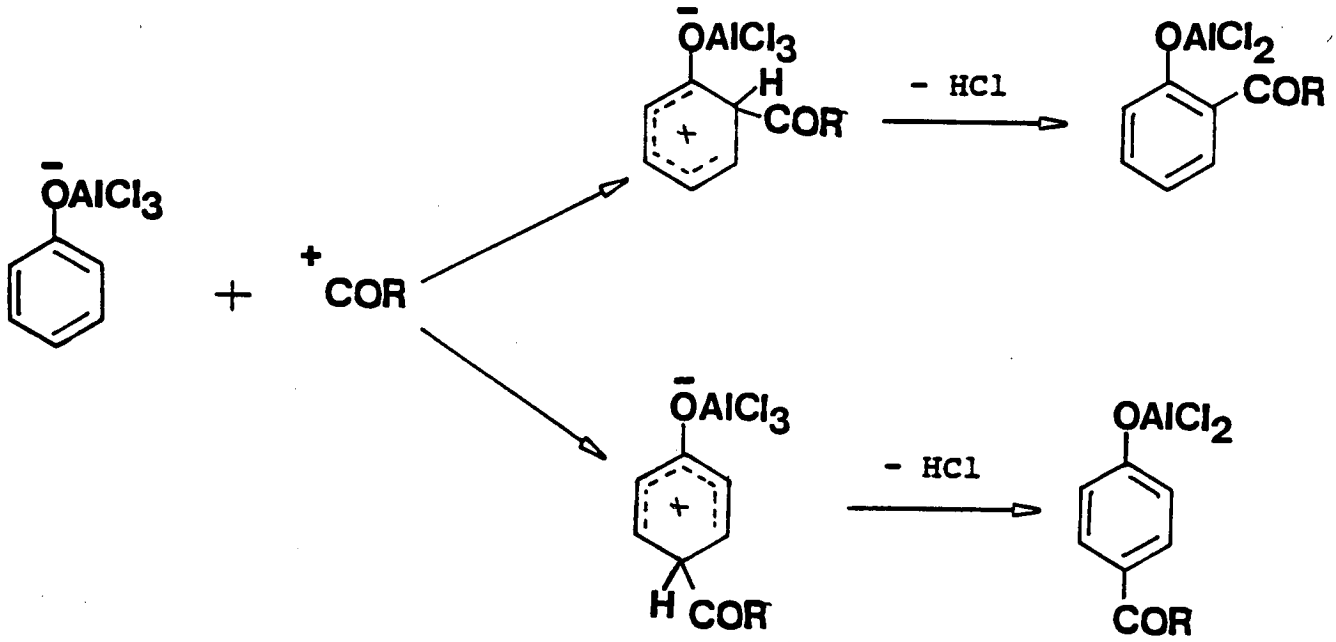
However, it has been demonstrated that transesterification can also take place under these conditions,[128] so the process is not necessarily proof of an intermolecular reaction. A bimolecular mechanism has also been supported by Hauser and Man,[129] who isolated the intermediate keto-ester [(19),R = C_6H_5] and showed that under the conditions of the Fries rearrangement, it was converted to the <u>para</u>-hydroxyketone product.

Auwers[128,130] considered the Fries rearrangement to be truly intramolecular from evidence that the rearrangement generally yielded more of the <u>ortho</u>-hydroxyphenyl ketone than the corresponding Friedel-Crafts reaction. More recently, Ogata

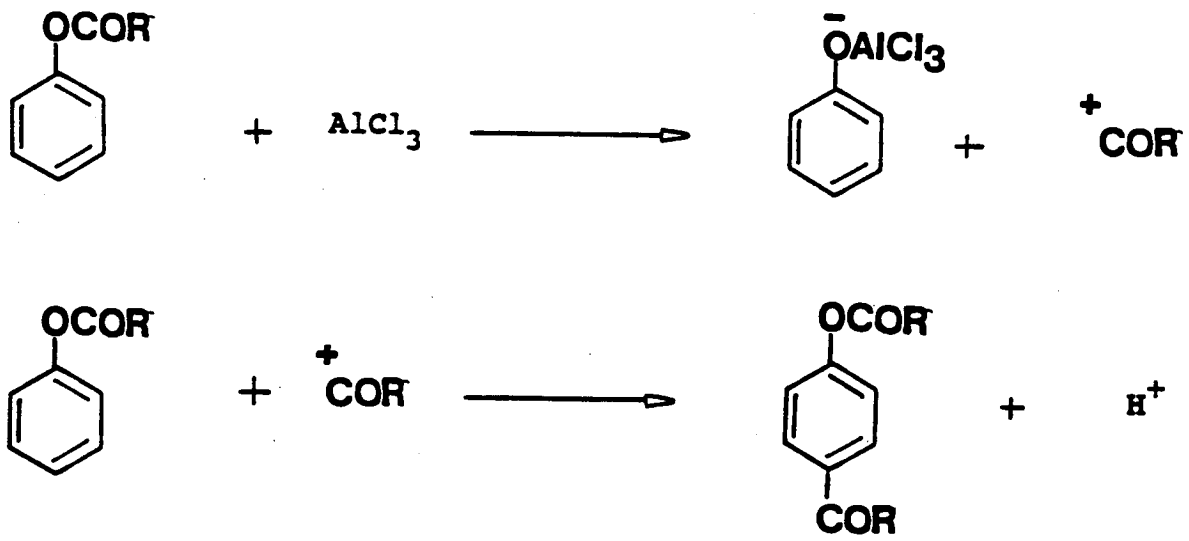
and Tabuchi[131] have endorsed an intramolecular pathway, based on a study of the rearrangement of phenyl acetate in the presence of 1-^{14}C acetic anhydride in a number of solvents. They proposed that the mechanism proceeded via a π-complex between the acyl cation and the phenoxytrichloroaluminium ion (Scheme 14). They suggest that this mechanism could yield both the ortho- and para- products.

These conflicting points of view suggest that the mechanism is neither exclusively inter- or intramolecular. Gerecs[75] has considered this and other evidence and has proposed that the inter- and intramolecular reactions are competitive processes in the Fries rearrangement. He has supported the view that the "para-rearrangement" is generally an intermolecular process and that the "ortho-rearrangement" is generally intramolecular, but is also possible intermolecularly. Evidence has come from experiments in which m-cresyl acetate was rearranged in the presence of diphenyl ether to yield the ortho- and para-hydroxyphenylketones and acylated diphenyl ether.[132] When the initial concentrations of m-cresyl acetate and diphenyl ether were lowered by a factor of five, the product concentrations of para-hydroxyketone and acylated diphenyl ether decreased by a similar factor. The ortho-hydroxyketone concentration remained the same. This suggests different mechanisms for the formation of para- and ortho- products - the para- intermolecularly by the same mechanism as acylation of the diphenyl ether and the ortho by an intramolecular process.

Scheme 11 (intermolecular)



Scheme 12 (bimolecular)



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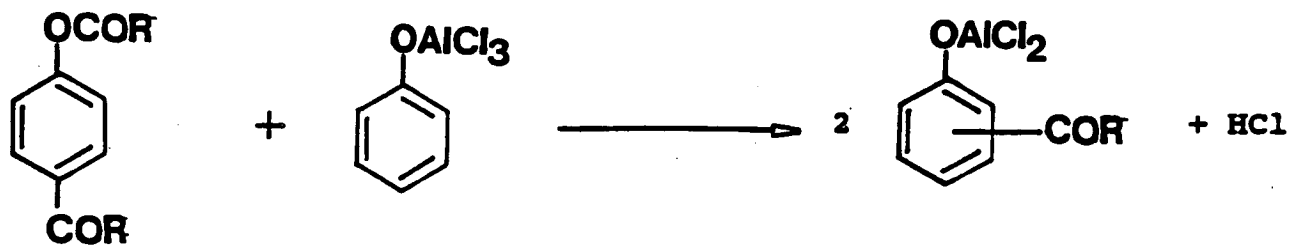
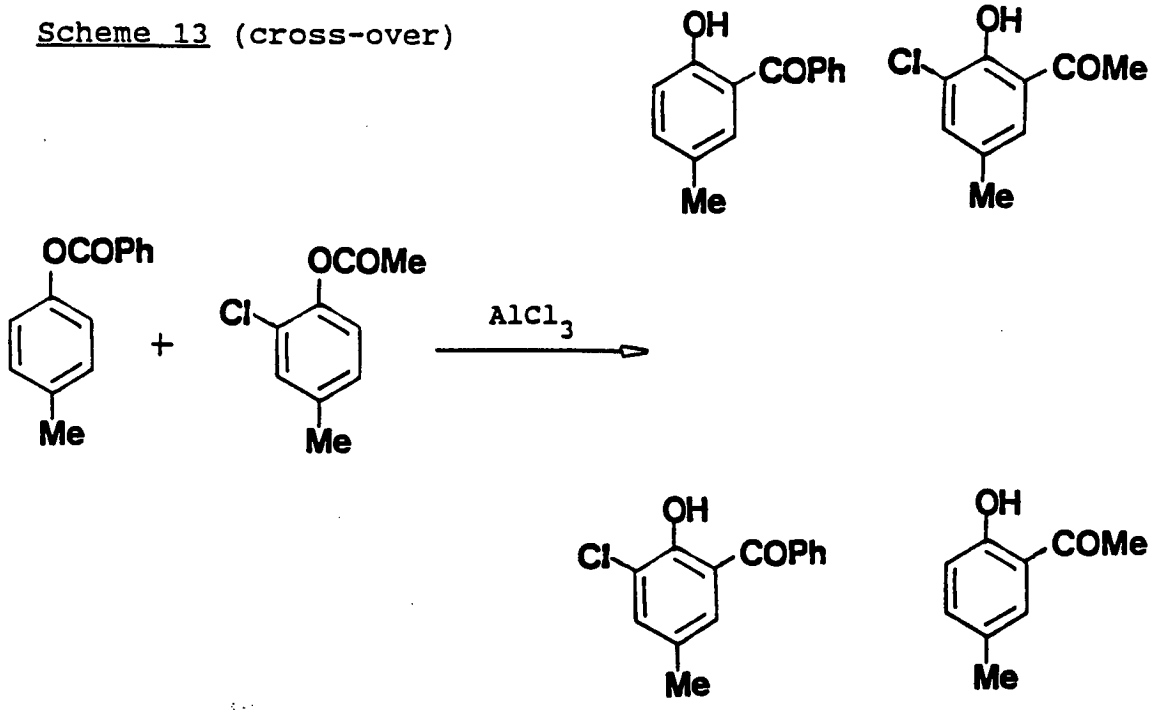
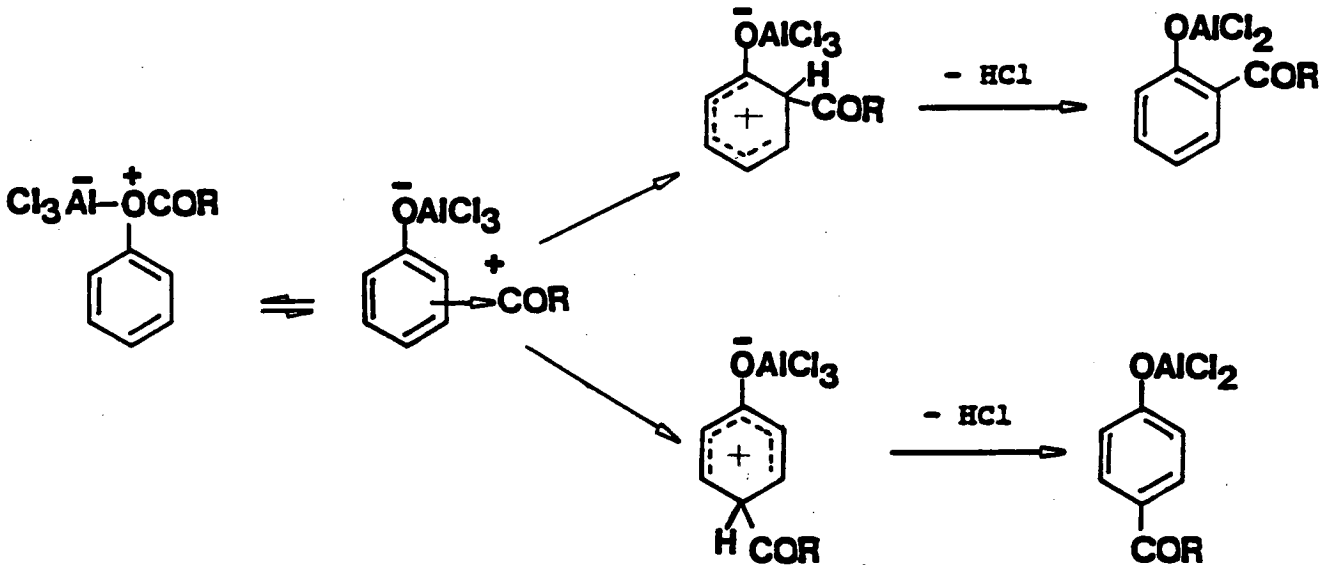


Scheme 13 (cross-over)



Scheme 14 (intramolecular)



3.1.4. Reversibility

Reversibility of the Fries rearrangement was initially reported by Rosenmund and Schnurr,[83] who found that para-hydroxyphenyl ketones with an alkyl group ortho to the acyl group were converted to the corresponding esters when heated with sulphuric or phosphoric acid. This conclusion was supported by Miguel[133] who reported the reverse rearrangement of similarly substituted para-hydroxyphenyl ketones in the presence of HCl and HBr. In contrast, Sullivan and Edwards[134] have maintained that rearrangement of these hydroxyketones is irreversible.

More recently, the conversion of hydroxyaryl ketones to the parent phenyl benzoate esters has been observed with trifluoromethanesulphonic acid as catalyst. This equilibrium process took place with both the ortho- and para- compounds, even when unsubstituted in the phenolic ring.

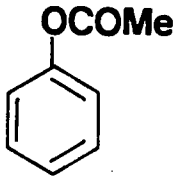
3.1.5 Applications of zeolites

The Fries rearrangement generally yields mixtures of ortho- and para-hydroxyphenyl ketones. It was considered that catalysis by zeolites might lead to enhanced para-selectivity because of the steric constraints imposed by the channels, with the additional advantage over Lewis acids of being re-usable.

For the present study on the effect of zeolites on the Fries rearrangement, phenyl acetate and phenyl benzoate were chosen as starting esters. To enable these reactions to be considered in the context of prior work, rearrangements of phenyl acetate

and phenyl benzoate catalysed by Lewis or Bronsted acids have been reviewed and tabulated (Tables 13 and 14). The tables illustrate the wide range of catalysts, reaction conditions and relative yields of ortho and para products which have been reported.

Table 13 reviews the conversion of phenyl acetate (20) to 2-hydroxyacetophenone [2-HAP(21)] and 4-hydroxyacetophenone [4-HAP(22)] and Table 14 the rearrangement of phenyl benzoate (23) to 2- and 4-hydroxybenzophenones [2-HBP (24), 4-HBP (25)]. In both, yields are expressed as mole percentages based on the starting material. Some of the entries have been selected as representative examples of a large number of reactions quoted in the original paper.[86,92,102] In some instances, yields of phenol and/or benzoic acid arising from hydrolysis of the ester were also reported[92,102,118] However, in most examples, there was no comment as to whether hydrolysis products were observed. Some papers have reported the yield of one isomer, but do not state whether the other isomer was also obtained. These instances have been identified in the tables.



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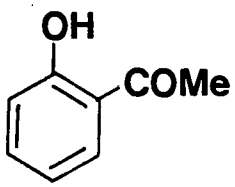

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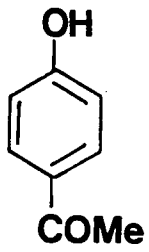

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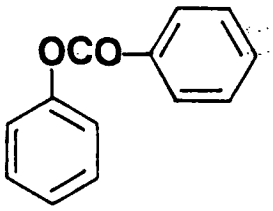

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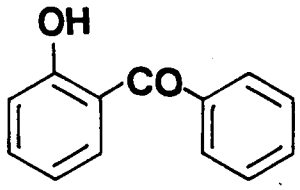

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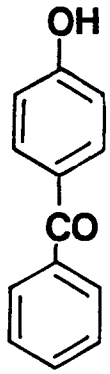


(25)

The different methods by which product yields were determined have also been noted. In recent papers, yields were found by gas chromatography (g.c.) or by integration of n.m.r. peaks. These results are likely to be more accurate than those reported in earlier papers where the products were isolated by techniques such as fractional crystallisation or steam distillation.

Prior to the commencement of the present work, only one example of a zeolite-catalysed Fries rearrangement had been reported in the literature.[139] This was a 1967 patent which covered gas phase reactions over low silica, X-type zeolites. Poor yields were obtained, with phenol the major product. With the development of high silica zeolites, the field of zeolite catalysis has greatly advanced, and it was considered that much better results would be obtained with these more recent materials.

Table 13 Fries rearrangement of phenyl acetate (literature)

entry	catalyst	catalyst: ester molar ratio[a]	T (^{o}C)	time	solvent	products (mol%) 2-HAP	4-HAP	para/ ortho ratio	ref
1	$AlCl_3$	2	60	5h	$PhNO_2$	11.4[b]	72.8[b]	6.4	92
2	$AlCl_3$	2	50	18h	$PhNO_2$	10.4[b]	76.5[b]	7.4	92
3	$AlCl_3$	1.6	120-165	20min	none	46.4[b]	41.7[b]	0.9	92
4	$AlCl_3$	1.3	60	4h	none	6.9[b]	11.3[b]	1.6	96
5	$AlCl_3$	1.3	165	-[c]	none	70[b]	-[c]	-	83
6	$AlCl_3$	1.2	20-25	24h	$PhNO_2$	-[c]	75[b]	-	83
7	$AlCl_3$	1.1	60-150	5h	CS_2	30[b]	-[c]	-	135
8	$AlCl_3$	1.1	20-25	27[d]	pet.ether	80[b]	8[b]	0.1	136
9	$AlCl_3$	1.1	100	25h	pet.ether	77[b]	15[b]	0.2	136
10	$AlCl_3$	2.0	120	7h	none	30[b]	-[c]	-	78
11	$AlCl_3$	1.25	120	1h	none	26[b]	38[b]	1.5	102
12	$TiCl_4$	1.6	120-165	20min	none	19.7[b]	14.9[b]	0.8	92
13	$TiCl_4$	2	60	5h	$PhNO_2$	11.3[b]	65.6[b]	5.8	92
14	$AlCl_3$-NaCl	5-2.3	180-200	2min	none	37[b]	35[b]	0.9	107
15	$ZnCl_2$	1	160	0.5h	none	7[b]	9[b]	1.3	102
16	$ZnCl_2$	1	130	1h	none	2.2[b]	10[b]	4.5	102
17	BF_3	1	100	1h	none	7[b]	54[b]	7.7	102

Table 13 continued

entry	catalyst	catalyst: ester molar ratio[a]	T (°C)	time	solvent	products (mol%) 2-HAP	4-HAP	para/ ortho ratio	ref
18	BF_3	1	180	5min	none	11[e]	26[e]	2.4	102
19	HF	20ml:10g[a]	20	24h	none	2[b]	77[b]	38.5	110
20	HF	20ml:10g[a]	100	1h	none	4[b]	75[b]	18.8	110
21	HF	20g:33g[a]	100	24h	pentane	-[c]	33[b]	-	113
22	PPA[f]	75:6.8g[a]	70-75	1.5h	none	-[c]	69[b]	-	114
23	PPA[f]	40g:6g[a]	100	10min	none	20[b]	53[b]	2.6	115
24	H_2SO_4	0.033	160	4h	none	2[e]	0.8[e]	0.4	102
25	$H_2SO_4.H_2O$	0.033	190	4h	none	20[e]	3[e]	0.2	102
26	H_3PO_4	0.033	160	4h	none	6[e]	2[e]	0.3	102
27	H_3PO_4	0.033	190	2.5h	none	8[e]	2[e]	0.2	102
28	CH_3SO_3H	0.033	160	4h	none	3[e]	trace[e]	-	102
29	CH_3SO_3H	0.033	190	3h	none	12[e]	2[e]	0.2	102
30	CH_3SO_3H	0.05	160	24h	none	22[e]	2[e]	0.1	102
31	$f\text{-}CH_3C_6H_4SO_3H$	0.033	160	4h	none	5[e]	0.7[e]	0.1	102
32	$f\text{-}CH_3C_6H_4SO_3H$	0.05	160	24h	none	25[e]	5[e]	0.2	102
33	$CH(SO_3H)_3$	0.033	160	4h	none	11[e]	3[e]	0.3	102
34	Dowex Resin	5 meq^{-1}: 1g[a]	150	4h	none	6[e]	4[e]	0.7	102

Table 13 continued

(a) molar ratio except where indicated
(b) isolated yield
(c) no information reported - product might be present
(d) yield determined by g.c.
(e) yield determined by n.m.r.
(f) PPA = polyphosphoric acid

Table 14 Fries rearrangement of phenyl benzoate (literature)

entry	catalyst	catalyst: ester molar ratio[a]	T (^{o}C)	time	solvent	products (mol%) 2-HBP	4-HBP	para/ ortho ratio	ref
1	$AlCl_3$	1.6	140	15min	none	27.4[b]	69.6[b]	2.5	92
2	$AlCl_3$	2	60	18h	$PhNO_2$	8.9[b]	80.5[b]	9.0	92
3	$AlCl_3$	1.3	63	4h	none	1.4[b]	19.5[b]	13.9	95
4	$AlCl_3$	1.2	140	15min	none	-[c]	100[b]	-	83,137
5	$AlCl_3$	1.1	98	5h	$PhNO_2$	8.6[b]	64[b]	7.4	132
6	$AlCl_3$	1.1	120	2h	$PhNO_2$	15[b]	54[b]	3.6	132
7	$AlCl_3$	3.1	190	7h	none	26[b]	-[c]	-	138
8	$AlBr_3$	1	110	2h	PhCl	9.6[d]	6.1[d]	0.6	86
9	$AlBr_3$	1	110	10h	PhCl	31.1[d]	30.7[d]	1.0	86
10	$AlBr_3$	2	110	2h	PhCl	24.9[d]	43.7[d]	1.8	86
11	$TiCl_4$	1.6	140	15min	none	23.1[b]	58.0[b]	2.5	92
12	$TiCl_4$	2	60	18h	$PhNO_2$	7.4[b]	83.7[b]	11.3	92
13	$AlCl_3$-NaCl	5-2.3	180-200	2min	none	17[b]	55[b]	3.2	107
14	$AlCl_3$-NaCl	3-1.5	140-200	2min	none	37.8[d]	50.2[d]	1.3	108
15	HF	150ml:76 mmol[a]	55	4h	none	"v.small"	70[b]	-	111
16	CF_3SO_3H	0.02	170	24h	$(Cl_2CH)_2$	39[d]	<2[d]	<0.1	118

Table 14 continued

entry	catalyst	catalyst: ester molar ratio[a]	T (^{o}C)	time	solvent	products (mol%) 2-HBP	4-HBP	para/ ortho ratio	ref
17	PPA[f]	220g:30g[a]	80	2.5h	none	-[c]	25[b]	-	116
18	PPA[f]	40g:6.6g[a]	100	10min	none	1[b]	6[b]	6.0	115
19	Nafion-H	100mg:10 mmol[a]	210	12h	$PhNO_2$	24[b,e]	48[b,e]	2.0	123
20	Nafion-H	0.05	150	4h	none	23[d]	33[d]	1.4	121

(a) molar ratio except where indicated
(b) isolated yield
(c) no information reported - product might be present
(d) yield determined by g.c.
(e) yield determined by n.m.r.
(f) PPA = polyphosphoric acid

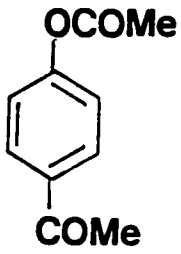
3.2 Results and Discussion

3.2.1 Fries Rearrangement of phenyl acetate

The effect of zeolites on the liquid phase Fries rearrangement of phenyl acetate has been investigated at temperatures of 170^{o} and 210^{o}C. Zeolite structure and acidity have been discussed in Chapter 1. Experiments were performed by stirring phenyl acetate with the catalyst in a 5:1 w/w ratio in the absence of a solvent. In selected examples, the progress of the rearrangement was monitored with time. Products were isolated from the zeolite in a centrifuge by repeated extraction with acetone. After drying the solution over magnesium sulphate and removal of the solvent under vacuum, the composition was determined by g.c. and/or h.p.l.c. Yields are presented as mole % based on starting material.

The conversion of phenyl acetate (20) to the Fries rearrangement products 2- and 4-hydroxyacetophenone [2-HAP (21), 4-HAP (22)] has been observed in the presence of acidic zeolites. In addition, phenol and 4-acetoxyacetophenone [4-AAP (26)] were identified in the reaction mixtures. Residual volatile acetic acid, arising from hydrolysis of phenyl acetate is considered to have been lost during the work-up procedure. By g.c., 4-AAP was obscured underneath the peak assigned to 4-HAP and its presence was confirmed by h.p.l.c. (by peak enhancement with an authentic sample). The corresponding ortho-isomer, 2-acetoxyacetophenone (2-AAP) was not detected. In the absence of zeolite no rearrangement products or phenol

were found after 52h at 210°C, and phenyl acetate was recovered in 92% yield.



(26)

Over H-Nu-2 at 170°C (Table 15), the highest yield of Fries rearrangement products was 2-HAP (3.7%), 4-HAP (11.6%) and 4-AAP (3.0%) after 30h. As 4-AAP presumably arises from acetylation of 4-HAP either by acetic acid or by transesterification with phenyl acetate, the tabulated para/ortho ratios incorporate the yields of both 4-HAP and 4-AAP. 4-AAP could also be formed by para-acylation of phenyl acetate. However, the ester group is deactivating to electrophilic aromatic substitution and this pathway would appear less favourable than acetylation at an acidic phenol group. A high degree of para-selectivity was observed throughout, but the combined para/ortho ratio was significantly greater at the start of the reaction and declined as it proceeded, from 10.3 at 0.5h to 3.0 at 52h. The profile of the reaction with time (Figure 13) shows fast conversion of phenyl acetate up to 1h, coinciding with rapid phenol formation (20.1% after 0.5h). This initial burst of phenol can be attributed to acid-catalysed hydrolysis of phenyl acetate in the presence of adventitious water in the

Table 15

Rearrangement of phenyl acetate over H-Nu-2 (170°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5	170	0.7	4.8	2.4	20.1	47.8	0.3	75.8
1		1.4	6.5	2.7	21.3	41.3	6.6	73.2
4		2.4	8.3	3.0	23.4	32.9	4.7	70.0
8		2.9	9.1	2.8	24.3	29.9	4.1	69.0
24		3.5	11.3	2.9	24.2	24.9	4.0	67.1
30		3.7	11.6	3.0	23.4	23.3	3.9	65.0
52		3.6	8.7	2.0	27.5	24.3	3.0	66.3

Table 16

Rearrangement of phenyl acetate over H-ZSM-5(H-Rblb) (170°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5	170	-	{0.1}		9.8	72.9	-	82.8
1		<0.1	0.3	<0.1	11.2	74.8	-	>86.2
4		0.2	1.2	0.5	12.2	69.0	8.5	83.1
8		0.4	1.3	0.8	12.5	69.2	5.2	84.2
24		0.9	2.8	2.1	13.1	65.2	5.4	84.1
30		1.5	3.2	2.4	14.7	62.7	3.7	84.5
52		1.5	2.6	2.4	14.9	61.2	3.3	82.6

Table 17

Rearrangement of phenyl acetate

catalyst	T (°C)	time (h)	2-HAP	(4-HAP+ 4-AAP) (mol%)	ph[a]	pa[b]	p/o	total
H-EU-1	170	24	1.2	1.5	11.6	63.8	1.2	78.1
H-Nu-10	210	54	1.0	1.1	8.7	73.5	1.1	84.3
Na-Y	170	24	-	-	22.3	76.0	-	98.3

a ph = phenol
b pa = phenyl acetate

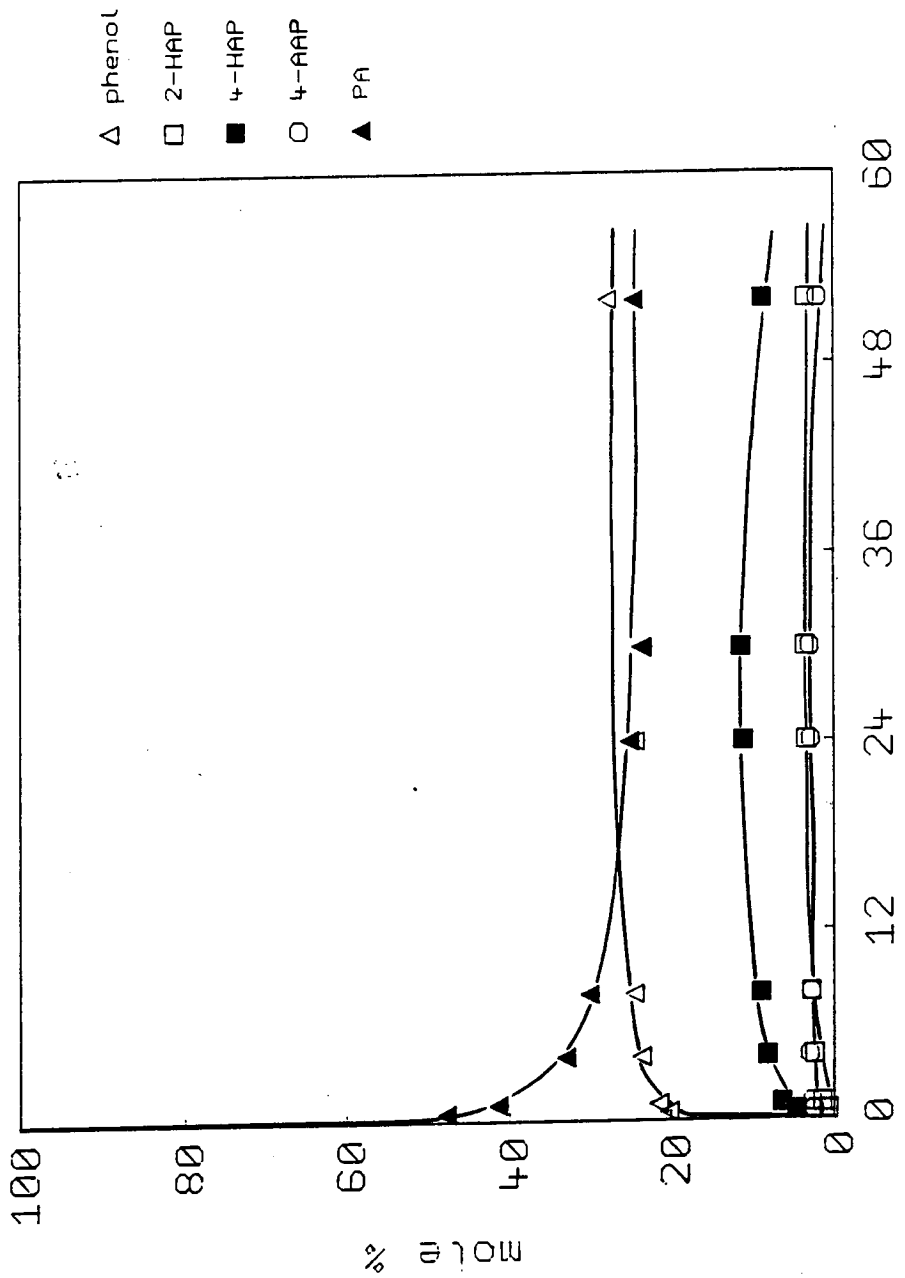


Figure 13 Fries rearrangement of phenyl acetate over H-Nu-2 at 170°C.

zeolite channels. A slight decrease in the yield of para-products (4-HAP and 4-AAP) between 30 and 52h was also observed.

The para-rearrangement was also favoured with H-ZSM-5 at 170°C (Table 16), but the overall conversion to Fries products was lower. After 30h the distribution was 2-HAP (1.5%), 4-HAP (3.2%) and 4-AAP (2.4%) and there was no further increase up to 52h (Figure 14). As with H-Nu-2, the para/ortho ratio dropped as the reaction progressed, from 8.5 at 4h to 3.3 at 52h.

When the same experiment was repeated over H-EU-1, lower yields were observed (Table 17). With Na-Y, a non-acidic zeolite, some hydrolysis took place but rearrangement products were not detected (Table 17).

In the zeolite-catalysed Claisen rearrangement (Section 2.2) it was shown that the conversion of allyl phenyl ether increased with zeolite acidity. A similar relationship applies to the Fries rearrangement (Table 18). Under the same conditions (170°C, 24h), H-Nu-2 gave significantly higher conversion of phenyl acetate (and yield of Fries products) than either H-ZSM-5 or H-EU-1. The results correlate with the low Si/Al ratio of H-Nu-2 and thus, high acidity.

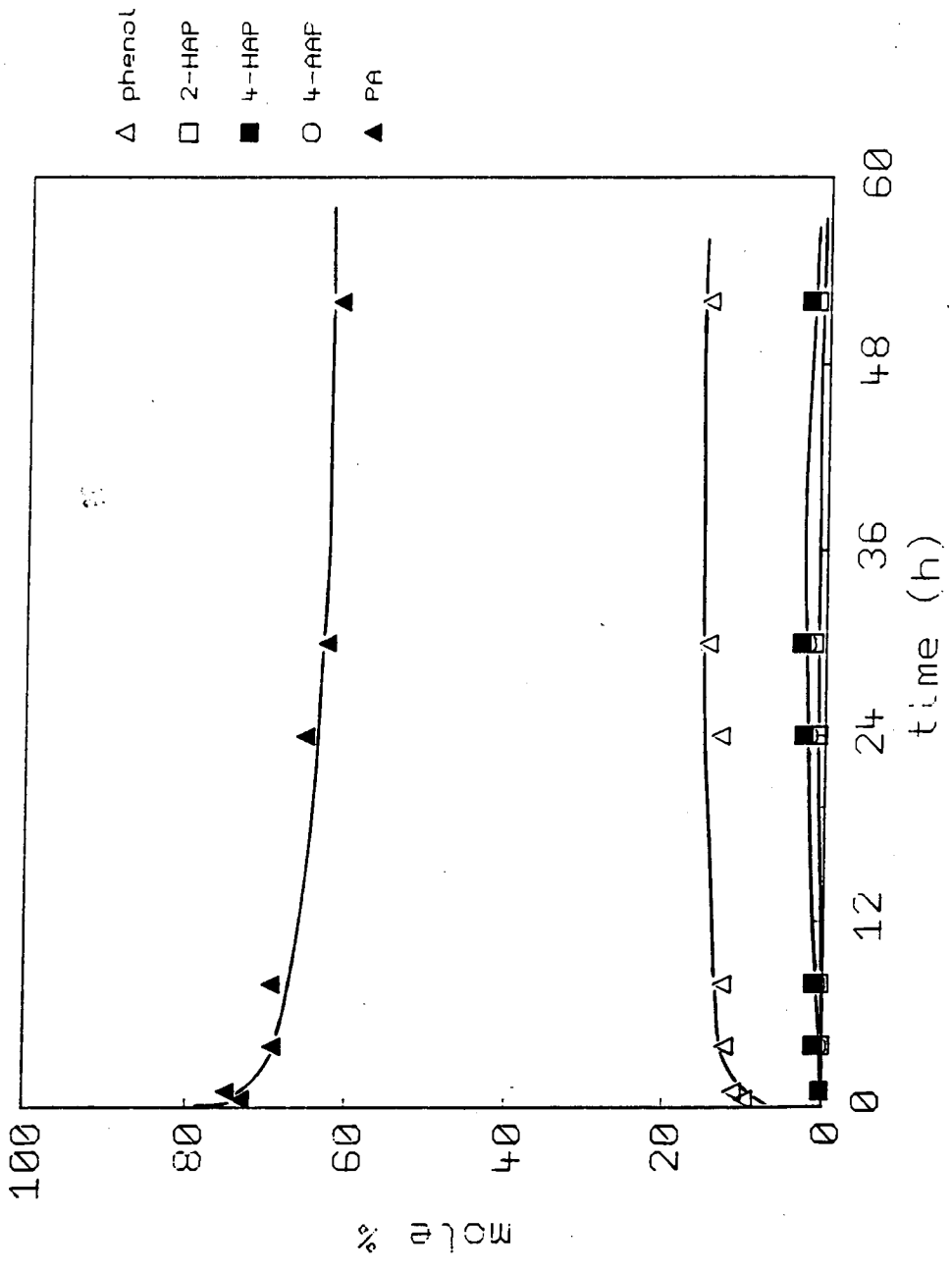


Figure 14 Fries rearrangement of phenyl acetate over H-ZSM-5 (H-Rb1b) at 170°C.

Table 18

Relationship between acidity and conversion over acid zeolites (170°C, 24h).

zeolite	Si/Al	% conversion phenyl acetate	% Fries products (2-HAP,4-HAP,4-AAP)
H-Nu-2	13.2	75.1	17.7
H-ZSM-5 (H-Rblb)	20.3	34.8	5.8
H-EU-1	21.9	36.2	2.7

In an attempt to improve the yield of Fries rearrangement products, the reactions over H-Nu-2 and H-ZSM-5 were repeated at 210°C (Tables 19 and 20). As in previous examples, para-orientation predominated and the para/ortho ratio became smaller as the reaction time increased. Over H-Nu-2, the initial yields of Fries products were markedly higher than at 170°C, but after 8h there was a significant decline in the quantity of these three products in the reaction mixture. Between 8 and 52h, the yield of 4-HAP dropped from 9.9 to 4.0%, 4-AAP from 3.5 to 0.7% and 2-HAP from 4.6 to 2.6% (Figure 15).

Over H-ZSM-5 conversion to products was enhanced at 210°C and, in contrast to H-Nu-2, there was no disappearance of these materials during reaction (Figure 16).

Table 19

Rearrangement of phenyl acetate over H-Nu-2 (210°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5	210	1.6	6.2	4.3	20.2	37.9	6.6	70.2
1		2.2	10.3	4.9	19.5	26.1	6.9	63.0
4		3.9	7.6	3.2	23.0	26.6	2.8	64.3
8		4.6	9.9	3.5	22.0	20.9	2.9	60.9
24		3.4	8.6	2.4	21.6	14.6	3.2	50.6
52		2.6	4.0	0.7	30.7	15.8	1.8	53.8

Table 20

Rearrangement of phenyl acetate over H-ZSM-5(H-Rblb) (210°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	Total
0.5	210	-	0.9	0.1	12.3	77.0	-	90.3
1		<0.1	1.2	0.3	13.4	75.3	-	90.2
4		0.2	1.9	0.8	14.2	72.8	13.5	89.7
8		0.9	2.2	1.4	15.4	71.0	4.0	88.7
24		3.3	5.4	4.1	17.4	60.3	2.9	85.1
52		4.6	6.4	4.4	19.1	54.0	2.3	88.5

Table 21

Rearrangement of phenyl acetate over regenerated H-Nu-2 (210°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
4	210	4.7	10.5	4.0	27.3	31.5	3.1	78.0
24		4 2	8.2	1.7	30.3	26.3	2.4	70.7
52		5.2	6.8	1.2	35.1	21.9	1.5	71.7

a ph = phenol
b ph = phenyl acetate

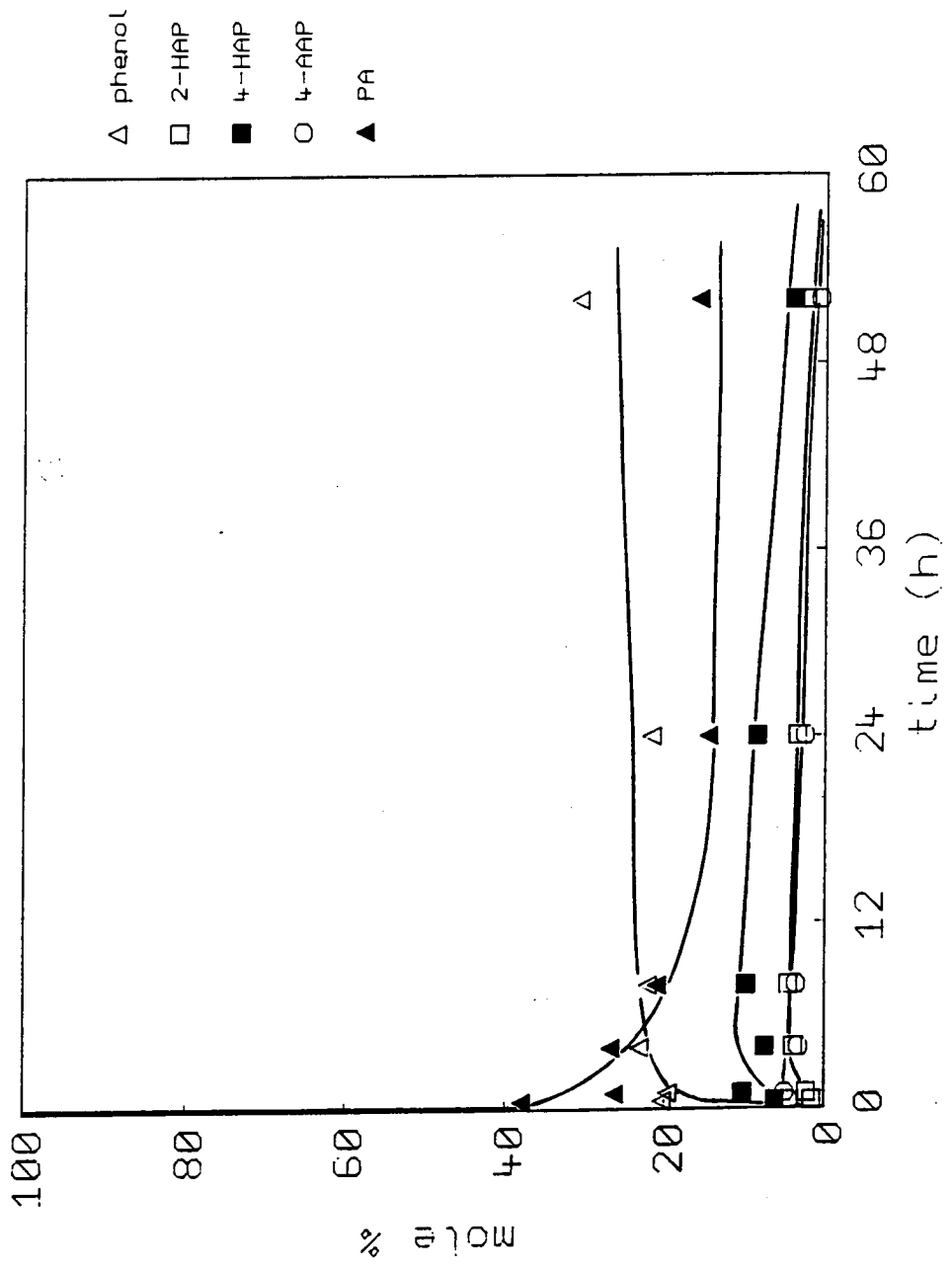


Figure 15 Fries rearrangement of phenyl acetate over H-Nu-2 at 210°C.

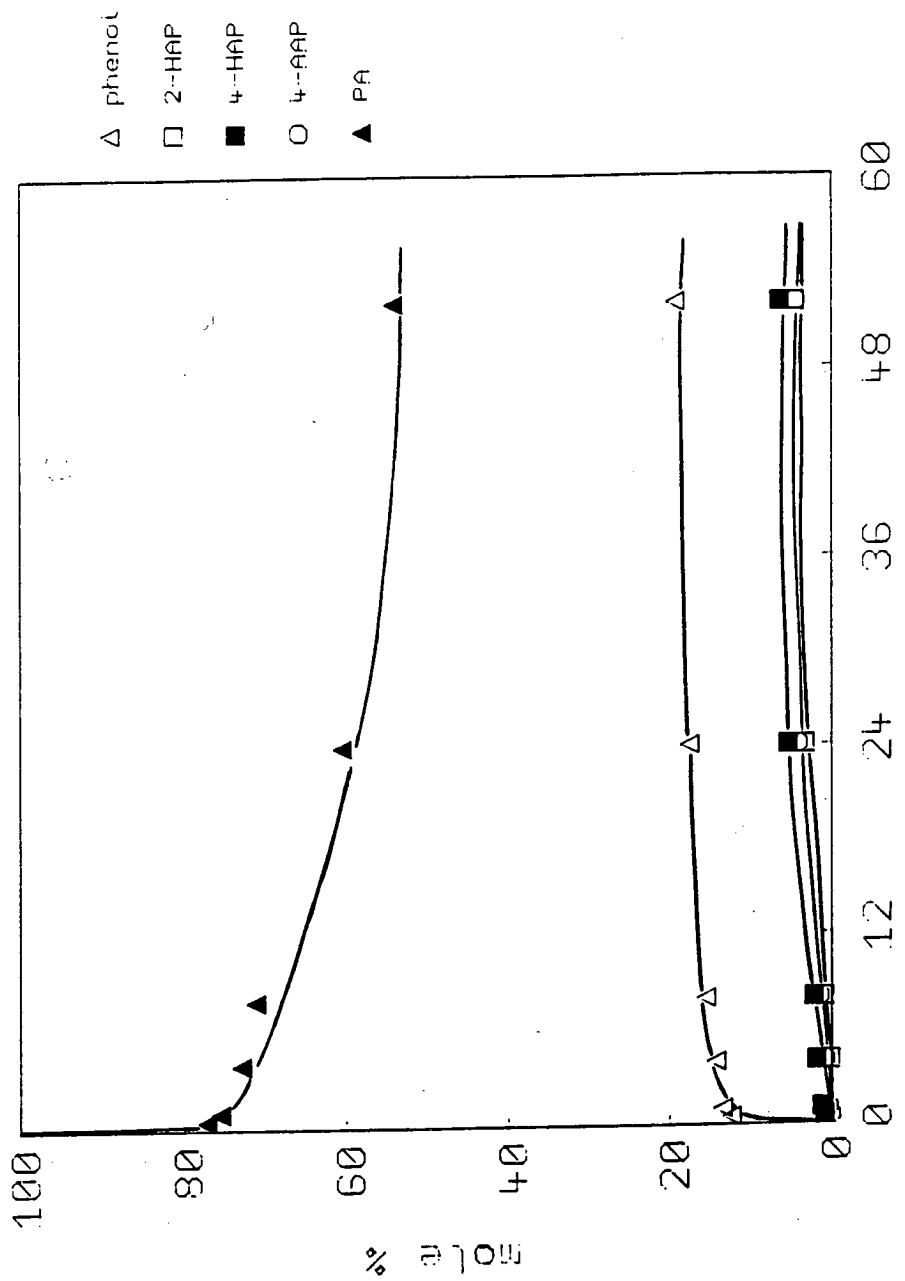


Figure 16 Fries rearrangement of phenyl acetate over H-ZSM-5 (H-Rb1b) at 210°C.

At 210°C the rearrangement was also attempted over H-Nu-10. Sorption of phenyl acetate by this material is unlikely because of the narrow channel diameters (Section 1, Table 1). After 54h, the products included 2-HAP (1.0%), 4-HAP and 4-AAP (1.1%), along with phenol and unchanged phenyl acetate (Table 17). The low yield and lack of selectivity suggest the starting material was not sorbed into the channels and the small amount of conversion was due to rearrangement on the zeolite crystal surfaces.

Thus the Fries rearrangement is promoted by acid zeolites. Furthermore, the reactions over the H-Nu-2 and H-ZSM-5 are catalytic as considerably more phenyl acetate was consumed than can be sorbed by the zeolite. For example, over H-Nu-2 at 170°C, the starting materials were phenyl acetate (7.51g) and H-Nu-2 (1.51g). As an approximate guide, t.g.a. indicated the water uptake of the H-Nu-2 to be 13.4% w/w at room temperature. A maximum of 0.20g of phenyl acetate would be sorbed by the zeolite, but after 52h, 75.7% of the ester was converted, i.e. 5.68g. Taking into account only the Fries products (2-HAP, 4-HAP, 4-AAP) because of extensive phenol formation, the yield was 14.5%, approximately 1.089g. As the yield is considerably greater than the maximum quantity sorbed by the zeolite, it is concluded that the reaction is catalytic.

During the rearrangements the zeolite and reaction mixture rapidly become discoloured and the rate of conversion of phenyl acetate decreases (Figures 13-16). This can be attributed to deactivation of the zeolite by coke formation. The catalyst can, however, be recovered, regenerated and re-used. After use, the sample of H-Nu-2 which gave the results in Table 19 was discoloured brown. It was regenerated as a clean white material by heating at 500^{o}C for 24h. When re-used, the product composition (Table 21) was similar to that previously observed. This result provides further evidence that the process is catalytic and the active sites can be regenerated.

Thus acid zeolites are re-usable, <u>para</u>-selective catalysts for the Fries rearrangement. The results can be compared with those obtained with Nafion-H, a polymeric, perfluorinated sulphonic acid resin which has been employed as a solid, superacid catalyst in organic synthesis.[69] It has been reported that the Fries rearrangement of aryl esters, including phenyl benzoate, is catalysed by Nafion-H but that attempts to rearrange the corresponding acetate esters were unsuccessful.[123] However, the present study has shown that Nafion-H does indeed promote the rearrangement of phenyl acetate under the reaction conditions employed with the zeolites. Furthermore, there is a marked contrast in selectivity between the non-porous Nafion-H and those reactions performed within the confines of the zeolite channels.

The rearrangement of phenyl acetate over Nafion-H at 170°C was monitored between 0.5 and 52h (Table 22). Under these conditions the greatest quantity of Fries products was observed after only 0.5h - 2-HAP (5.1%), 4-HAP (4.3%), 4-AAP (0.8%) and there was a small, but steady, decline in the yield of each product up to 52h. Whereas the zeolite-catalysed reactions were highly para-selective, Nafion-H afforded almost equal quantities of ortho- and para- products. In fact, there was a slight trend towards ortho- selectivity with increasing reaction time. The ratio of 4-HAP to 4-AAP is much greater than in the zeolite-catalysed reactions which would suggest that transesterification occurs more readily within the steric confines of the zeolite channels. The low mass balance indicates that further side reactions or decomposition may occur.

When the product selectivity in the H-Nu-2, H-ZSM-5 and Nafion-H reactions at 170°C is compared (Figure 17) it is clear that the zeolites yield high initial para/ortho ratios which decline with increasing reaction time. The comparable Nafion-H system shows no marked selectivity. Up to 24h, H-ZSM-5 appears to yield the highest proportion of para- products. For example, after 4h, the para/ortho ratios with H-ZSM-5, H-Nu-2 and Nafion-H are 8.5, 4.7 and 1.1 respectively. However, at 4h, the conversion of initial phenyl acetate to products is considerably less over H-ZSM-5 than H-Nu-2. When the yield of Fries products is taken into account, the reactions with H-Nu-2

Table 22

Rearrangement of phenyl acetate over Nafion-H (170°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5	170	5.1	4.3	0.8	27.9	23.8	1.0	61.9
1		5.1	4.2	0.7	26.7	21.2	1.0	57.9
4		4.4	4.1	0.6	25.3	15.2	1.1	49.6
24		4.2	3.1	0.2	27.3	12.6	0.8	47.4
52		4.4	2.9	0.2	31.9	11.5	0.7	50.7

Table 23

Rearrangement of phenyl acetate over (Cu(II),H)-Y (210°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5	210	-	-	-	34.7	58.6	-	93.3
1		-	{0.1}		34.7	58.0	-	92.7
4		0.2	0.8	0.2	36.2	57.1	5.0	94.5
24		0.7	1.8	0.5	38.1	53.0	3.3	97.4
30		0.9	2.0	0.6	39.9	52.7	2.9	96.1
52		1.0	2.2	0.6	36.3	45.8	2.8	85.9

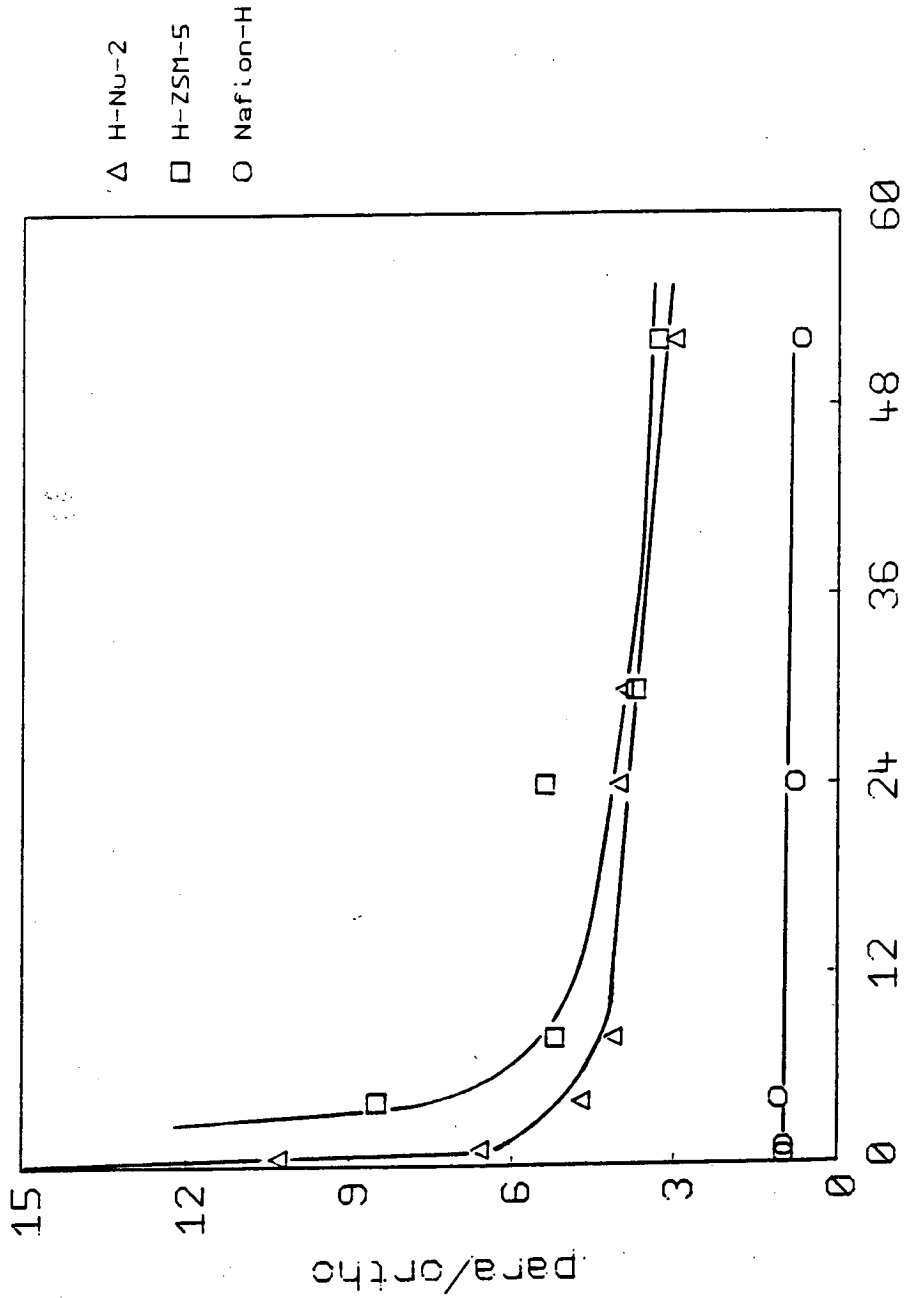
Table 24

Rearrangement of phenyl acetate over pre-dried H-Nu-2 (170°C)

time (h)	T (°C)	2-HAP	4-HAP	4-AAP (mol%)	ph[a]	pa[b]	p/o	total
0.5		2.0	8.6	2.1	9.6	70.4	5.4	92.7
1		3.0	14.8	4.0	11.1	56.2	6.3	89.1
24		5.6	13.6	1.9	17.4	50.2	2.8	88.7
52		5.6	8.3	2.6	18.2	48.7	1.9	83.4

a ph = phenol
b pa = phenyl acetate

Figure 17 Product selectivity versus reaction time in Fries rearrangement of phenyl acetate(170°C)

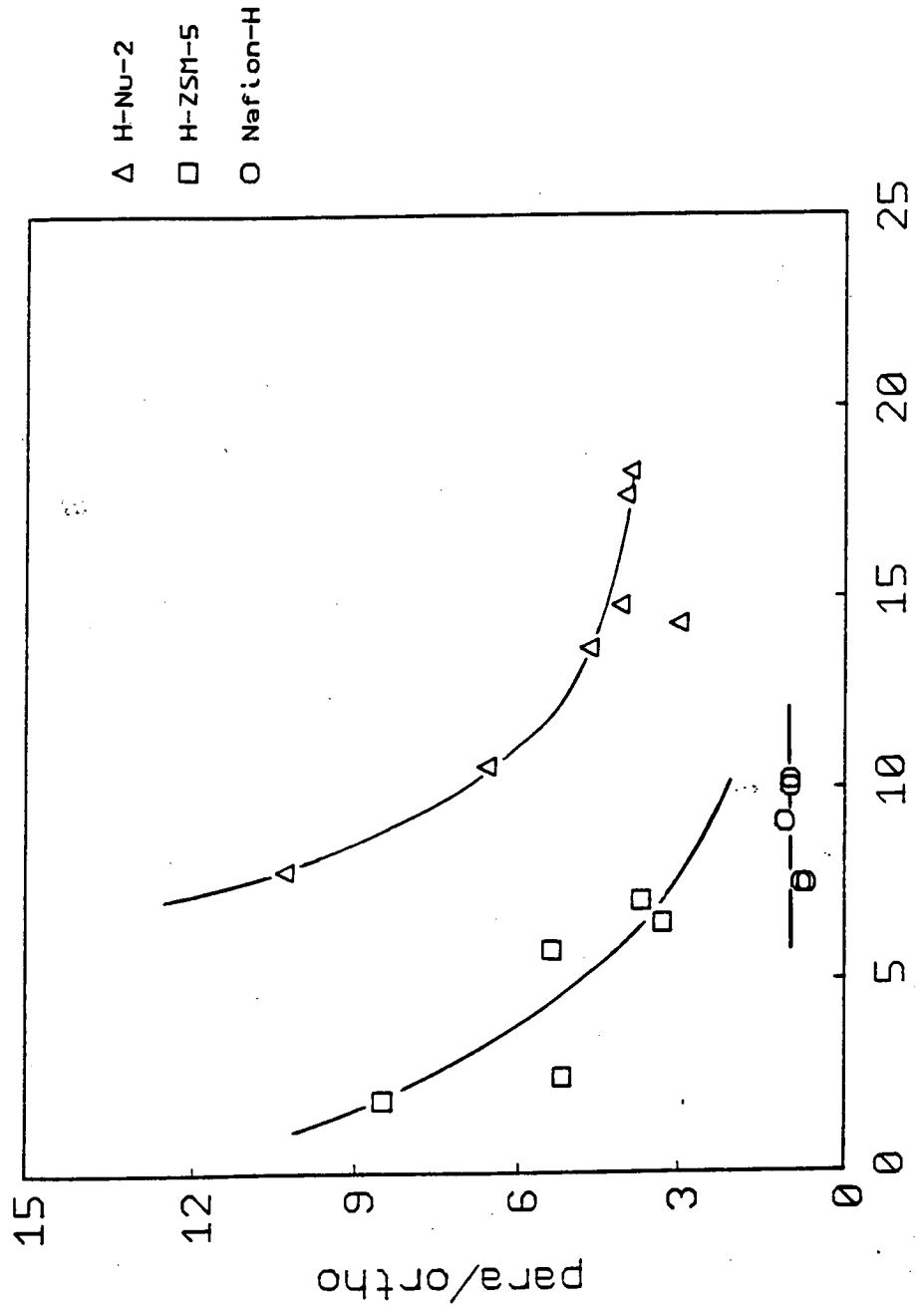


are more para- selective (Figure 18). For example, for an overall yield of 8% the para/ortho ratios of H-Nu-2, H-ZSM-5 and Nafion-H are 7, 3 and 1 respectively. Thus extremely high para- selectivity would be predicted at low conversions over H-Nu-2.

Acid zeolites also exhibit greater selectivity towards 4-HAP than comparable Lewis and proton acid-catalysed rearrangements of phenyl acetate (Table 13). At 165°C, aluminium chloride afforded a 70% yield of 2-HAP (Table 13, entry 14). In general, Lewis acids favour para- formation at low temperatures and ortho- formation at high temperatures. With BF_3, a para/ortho ratio of 2.4 was observed after 5 mins (entry 18), but this is much lower than would be predicted with H-Nu-2 for the same reaction time (Figure 17). Without exception, proton acids are reported to be ortho-selective (Table 13 entries 24 to 34). Thus it can be concluded that it is the restrictions of the zeolite channels which give rise to para- selectivity.

The higher proportion of para- products from H-Nu-2 than H-ZSM-5 (Figure 18) might be attributed to the greater acidity of this material. An intermolecular pathway is generally accepted for the formation of 4-HAP via acid-catalysed cleavage of phenyl acetate to phenol and the acyl cation with subsequent aromatic substitution at the para-position. The higher acidity of H-Nu-2 would favour this process. However, it has been reported[69] that the acidity of Nafion-H is comparable to that of 100% sulphuric acid which would suggest that Nafion-H is

Figure 18 Product selectivity versus % yield Fries products in Fries rearrangement of phenyl acetate (170°C)



more acidic than high silica H-Nu-2. The lack of selectivity in the Nafion-H system suggests that it is the difference in pore structure between H-Nu-2 and H-ZSM-5 which accounts for the contrasting para/ortho ratios. The larger H-Nu-2 channels may provide the required freedom for cleavage and aromatic substitutions than the narrower channels of H-ZSM-5 (Section 1.1, Table 1).

Catalysis of the Fries rearrangement by acid zeolites can be attributed to Bronsted sites (Section 1.1). As the reaction is traditionally promoted by Lewis acids, the effect of introducing Lewis acid ions into the zeolite structure was examined.

The effect of (Cu(II),H)-Y (composition as in Section 2, Table 10) on the rearrangement of phenyl acetate was monitored with time at 210°C (Table 23). The yield of Fries products was low [2-HAP (1.0%), 4-HAP (2.2%), 4-AAP (0.6%) after 52h], but as in previous examples the reaction was para- selective. Phenol formation was a strongly competing side reaction (36.1% after 30h) reflecting the high water sorption capacity of this material (25.7% by t.g.a.). Under these conditions, (Cu(II),H)-Y is a less efficient catalyst than either H-Nu-2 or H-ZSM-5.

The role of the Cu(II) ion is not clear as a sample of H-Y for comparison could not be prepared. A number of attempts to make it via calcination of NH_4-Y were unsuccessful. The higher mass

balance in this system than with H-ZSM-5 or H-Nu-2 suggests that side reactions may be promoted by proton acid sites.

Phenol formation was an unwanted side reaction in all the zeolite-catalysed Fries rearrangements. In an attempt to eradicate water from the system and thus prevent hydrolysis of phenyl acetate, the process was repeated over H-Nu-2 under scrupulously dry conditions. The zeolite was dried at 400°C for 17h, cooled in a vacuum desiccator over phosphorus pentoxide, transferred to the reaction vessel under dry nitrogen and further dried at 170°C under 0.1mm Hg vacuum before use (Table 24). The yield of phenol was considerably reduced in the dried reaction. In comparison to the previous reaction over H-Nu-2 at 170°C (Table 15) slightly enhanced yields were observed and the products formed more rapidly, presumably as less phenyl acetate is converted to phenol. After 0.5h the dried H-Nu-2 gave 2-HAP (0.7%), 4-HAP (4.8%) and 4-AAP (2.4%) compared to yields of 2.0, 8.6 and 2.1% respectively when the zeolite was not pre-dried.

The largest quantity of phenol observed in the "dry" reaction was 18.2%. If it is assumed that 4-AAP is formed by the transesterification reaction between phenyl acetate and 4-HAP, 4.0% phenol is the maximum formed in this process. Thus 14.2% phenol remains to be accounted for. Either residual water remained in the zeolite despite the precautions employed, or some alternative mechanism(s) for phenol formation operate. A yield of 14.2% phenol in the product mixture corresponds to

0.008 moles water in the zeolite at the start of the reaction. In 1.5g H-Nu-2 this is 9.4% by weight. By t.g.a. the water uptake of H-Nu-2 was 13.45%. If all the phenol was produced by hydrolysis, only 30% of the original sorbed water in the zeolite was removed by the drying procedures.

Formation of phenol in the H-Nu-2 and H-ZSM-5 systems is greater than would be predicted even if both hydrolysis and transesterification occur. In a typical experiment, utilising 1.5g H-Nu-2 at 170^{o}C, there would be 0.011 moles of water present in the zeolite. Of the initial phenyl acetate (7.5g, 0.055 moles), 0.011 moles would be converted to phenol, ie. a maximum of 20.3% by hydrolysis. The greatest yield of 4-AAP was 3.0%, thus taking transesterification into account the maximum theoretical yield of phenol would be 23.3%. However, the experimental yield was 27.5%. The same procedure has been applied to H-ZSM-5 and (Cu(II),H)-Y (Table 25).

Table 25

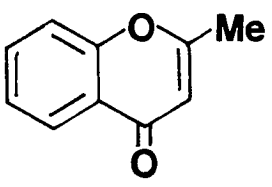
Phenol formation over zeolites - theoretical and experimental yields.

zeolite	%H_2O t.g.a. (w/w)	T (^oC)	max ph.[a] by hydrol. (mol%)	max ph.[a] by tran. (mol%)	total theory ph.[a] (mol%)	exptl. (mol%)
H-Nu-2	13.45	170	20.3	3.0	23.3	27.5
		210	20.3	4.9	25.2	30.7
H-ZSM-5 (H-Rblb)	7.79	170	11.8	2.4	14.2	14.9
		210	11.8	4.4	16.2	19.1
(Cu(II),H)-Y		210	38.8	1.0	39.8	36.3

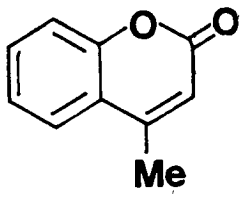
a ph = phenol

Over H-Nu-2 at 170^oC and 210^oC and H-ZSM-5 at 210^oC, the experimental yield of phenol was significantly greater than the predicted yield. This observation suggests that side reactions apart from hydrolysis and transesterification occur which give rise to phenol (or water). The low mass balances in zeolite-catalysed Fries rearrangements also indicate that competitive side reactions may occur.

By g.c. analysis, a number of products in addition to the Fries products were detected (Table 26). Two small peaks eluted immediately after the Fries products were identified as 2-methylchromone (27) and 4-methylcoumarin (28) by g.c.-m.s. ($^m/_Z$ (M^+) 160) and peak enhancement with the authentic materials.



(27)



(28)

In addition to these cyclic materials, some large, broad peaks were observed at high temperature and long elution times, and were attributed to high boiling products. The molecular weights could not be satisfactorily determined by g.c.-m.s. because of the long elution time and poor resolution.

Table 26

Additional products

zeolite	T(^{o}C)	2-MCH[a]	4-MC[b]	High T broad peaks
H-Nu-2	170	-	-	+
	210	+	+	+
H-ZSM-5(H-Rblb)	170	-	-	-
	210	-	-	-
(Cu(II),H)-Y	210	-	-	-
H-Nu-2 (dried)	170	-	-	+
Nafion-H	170	-	-	+

a - 2-methylchromone
b - 4-methylcoumarin

+ = detected
- = not detected

2-Methylchromone and 4-methylcoumarin were only detected over H-Nu-2 at 210^{o}C in a combined yield of less than 1%. It is considered likely that they were formed by the intramolecular

condensation of 2-AAP, thus explaining the absence of this material in the reaction mixtures. However, when 2-AAP was heated with H-Nu-2 in a 1.5:1 w/w ratio, at 210°C for 52h, only traces of these products were detected. The result suggests that cyclisation does not readily occur under these conditions. Indeed, the major product was 2-HAP, and 2-AAP was not recovered. When the reaction was attempted by pre-sorption of 2-AAP into the zeolite, and in the presence of acetic acid, the same result was obtained. Alternative pathways which were investigated include the condensation between 2-HAP and phenyl acetate and the reaction of 2-HAP with acetic acid but these were unsuccessful.

The possibility of reverse rearrangement of the ortho- and para-hydroxyketone products or of isomerism between the two has been examined (Table 27). The Fries rearrangement of aryl benzoates is reported to be an equilibrium process.[119] When 4-HAP was heated with H-Nu-2 at 210°C for 24h in the absence of solvent, very small quantities of phenyl acetate and 2-HAP were detected, which were not present in the starting material. With 2-HAP as starting material no other products except for phenol were detected. Thus, the zeolite-catalysed rearrangement does not appear to be readily reversible unless phenyl acetate is hydrolysed as it is produced to form the observed phenol. An alternative mechanism for the high yields of phenol in these reactions would involve an unusual aromatic substitution with H^+ replacing ^+COMe. Either of these pathways

Table 27

Attempted reverse rearrangements

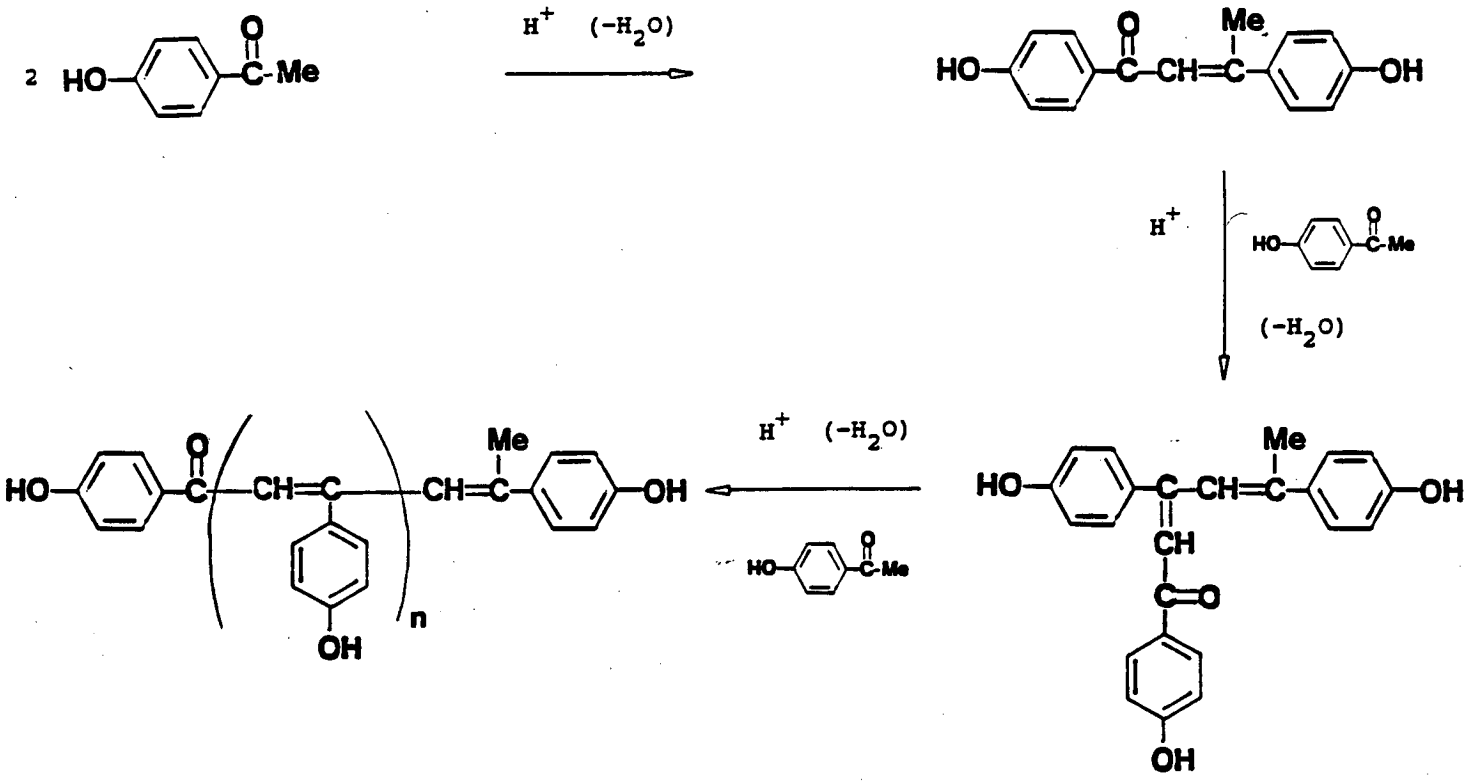
phenol	T (°C)	time (h)	2-HAP	(4-HAP+ 4-AAP[c]	ph[a]	pa[b]	total
				mol%			
2-HAP	210	24	64.3	-	6.0	-	70.3
4-HAP	210	24	0.2	17.0	23.6	<0.1	40.8

a ph = phenol
b pa = phenyl acetate
c presence of 4-AAP not confirmed

may contribute to the large quantities of phenol in the zeolite-promoted Fries rearrangements.

In the above reverse reactions (Table 27) mass balances were low and the products were tarry and discoloured. It is proposed that the hydroxyketones, 2- and 4-HAP, might undergo acid-catalysed aldol condensation under the reaction conditions leading to high molecular weight poly-condensation products (Scheme 15).

Scheme 15

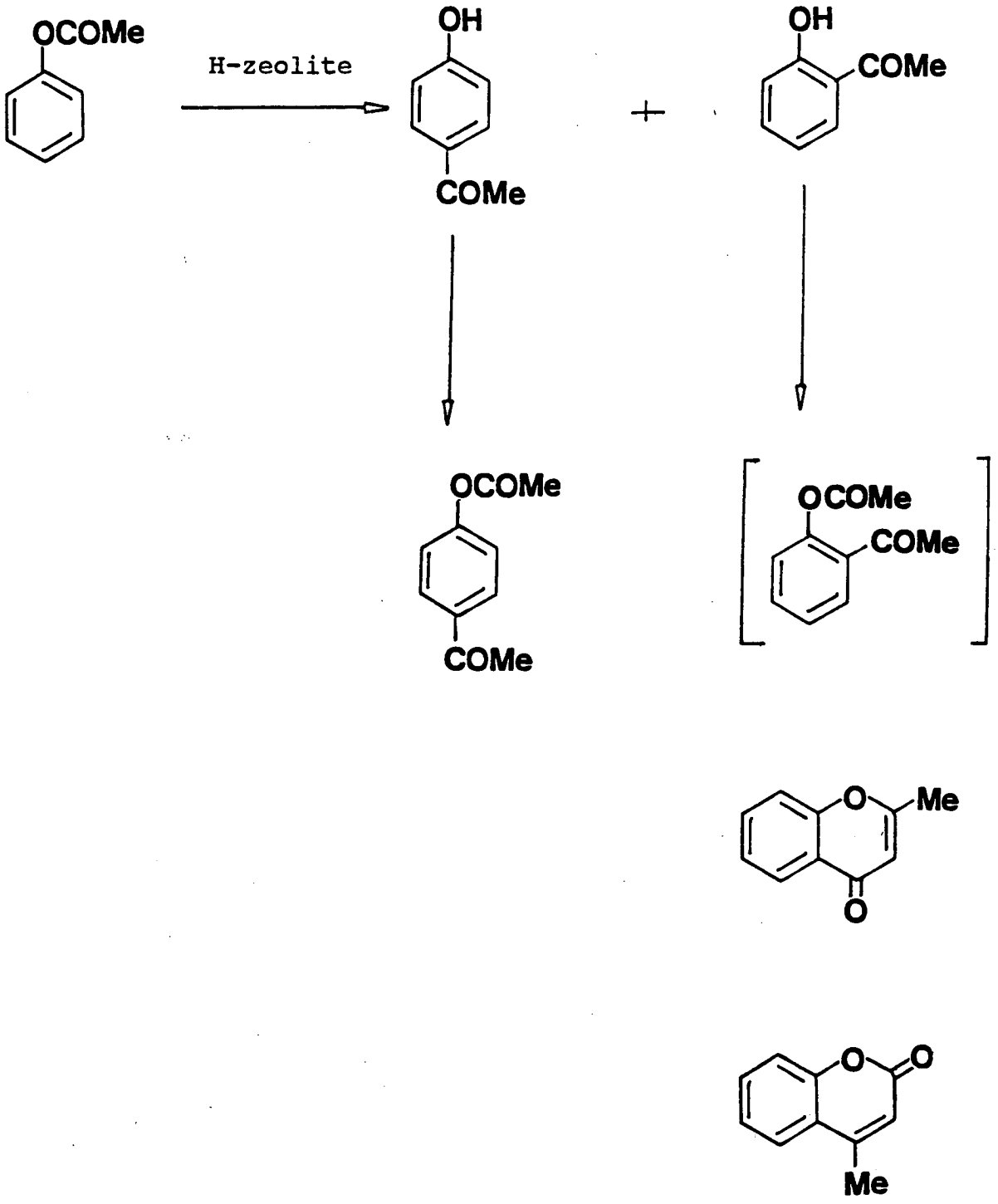


Indeed, studies on a model acetophenone system (Section 4) have shown that the aldol condensation can be effected by H-Nu-2. This is a potential pathway to account for the disappearance of para-substituted products and the low mass balances in the zeolite-catalysed systems. Water evolved may contribute to phenol formation. A similar process can be envisaged with 4-AAP. 4-HAP and 4-AAP are lost more rapidly than 2-HAP, presumably because of hydrogen bonding in the ortho-hydroxyketone. This may prevent reaction at the hydroxy function and thus explain the absence of 2-AAP in the reaction mixtures.

During the course of this study, a gas-phase Fries rearrangement of phenyl acetate[140] was reported over H-Y and H-ZSM-5. The results were in contrast to the liquid phase reactions examined here. At 400°C, 2-HAP was the major product. The ten-fold increase in para/ortho ratio with H-ZSM-5 was attributed to shape-selectivity, although the relative acidity of the zeolites was not considered.

In conclusion, acid zeolites are para-selective catalysts for the Fries rearrangement. In contrast to traditional Lewis acid systems, a number of side reactions were observed. With $AlCl_3$ complexation presumably prevents the formation of additional products. The zeolite-catalysed reactions are summarised in Scheme 16.

Scheme 16


OCOMe
H-zeolite
OH
COMe
OH
COMe
OCOMe
COMe
OCOMe
COMe
O
Me
O
O
O
Me

3.2.2 Fries rearrangement of phenyl benzoate

Two methods were employed to examine the Fries rearrangement of phenyl benzoate (23) over zeolites at 210°C and 140°C. In the first, phenyl benzoate was stirred with the catalyst in a 5:1 w/w ratio in the absence of a solvent, i.e. molten phenyl benzoate. In an alternative procedure, the solid phenyl benzoate was sorbed onto the zeolite in a 1:1 w/w ratio by dissolving in methylene chloride, stirring in the zeolite and subsequent slow removal of methylene chloride under vacuum. A similar procedure has been reported for the photolysis of dibenzyl ketones.[28] The dry powder was then heated to effect rearrangement.

In both methods, the products were isolated from the zeolite in a centrifuge by repeated extraction with acetone. After drying the product solution over magnesium sulphate and removal of the solvent under vacuum, the product composition was determined by g.c. Yields are presented as mole % based on starting material. Yields of recovered phenyl benzoate, 2-hydroxybenzophenone [2-HPB,(24)], 4-hydroxybenzophenone [4-HBP(25)] and phenol are recorded. While benzoic acid was detected by g.c., yields are not presented here as it gave a long, tailing peak under the analysis conditions employed and could not be accurately quantified.

When phenyl benzoate was stirred with H-Nu-2 at 210°C, significant conversion to 2-HBP and 4-HBP was observed, along with phenol (Table 28). The process is slightly para-

selective after 0.5h, but the para/ortho ratio decreases and the rearrangement is ortho- selective at 72h. In the absence of catalyst, phenyl benzoate was recovered in quantitative yield and no other products were detected (Table 29). In addition, over Na-Y, a non-acidic, large pore zeolite of similar pore size to H-Nu-2 there was no conversion to Fries products although there was some phenol formation.

Over medium pore acid zeolites, H-ZSM-5 and H-EU-1, only traces of Fries products were detected (Table 29). The phenyl benzoate starting material is probably too bulky to be sorbed into these channel structures. Over H-ZSM-5, the small amount of rearrangement which does occur is likely to take place on the zeolite external surfaces.

Table 28 Rearrangement of phenyl benzoate over H-Nu-2 (stirred, 210°C)

time (h)	T (°C)	2-HBP	4-HBP	ph[a]	pb[b] (mol%)	p/o	total[c]
0.5	210	3.8	5.2	18.3	61.4	1.4	88.7
1		6.0	10.3	21.0	46.3	1.7	83.6
4		12.7	15.1	20.6	35.3	1.2	84.9
24		24.5	10.1	18.7	25.6	0.4	78.9
48		24.9	11.3	21.4	24.9	0.4	82.5
72		24.5	8.4	25.0	23.0	0.3	80.9

Table 29 Rearrangement of phenyl benzoate (stirred, 210°C)

catalyst	T (°C)	time (h)	2-HBP	4-HBP	ph[a]	pb[b]	p/o	total[c]
H-ZSM-5 (SKH-Z2)	210	72	<0.1	<0.1	9.5	68.2	-	>77.9
(Cu(II),H)-Y	210	72	2.0	1.2	23.4	32.1	0.6	58.7
Na-Y	210	72	-	-	23.1	45.6	-	68.7
None	210	72	-	-	-	100.3	-	100.3
H-EU-1	210	72	-	<0.1	8.3	55.8	-	>64.2

Table 30 Rearrangement of phenyl benzoate over Nafion-H (stirred, 210°C)

time (h)	T (°C)	2-HBP	4-HBP	ph[a]	pb[b] (mol%)	p/o	total[c]
0.5	210	11.5	10.0	15.5	35.5	0.9	72.5
1		15.3	10.2	16.3	27.2	0.7	69.0
4		19.9	8.9	15.7	22.6	0.4	67.1
24		19.0	7.4	15.9	18.6	0.4	60.9
48		17.7	7.0	17.2	17.0	0.4	58.9
72		15.2	5.6	18.5	14.5	0.4	53.8

a ph = phenol
b pb = phenyl benzoate
c benzoic acid detected but not quantified

Over non-porous Nafion-H[69] acidic, perfluorinated resin at 210°C (Table 30), 2-HBP and 4-HBP were observed but yields were lower than over H-Nu-2 under the same conditions (Table 28). In addition, the para-selectivity was lower as a function of time than in the corresponding reaction over H-Nu-2.

The above experiments over zeolites were repeated, employing the sorption technique instead of stirring phenyl benzoate with the zeolite (Table 31). The para/ortho ratios obtained by this method over H-Nu-2 after 24h are very similar to those in the stirred reaction (Table 28).

The Fries rearrangement of phenyl benzoate over H-Nu-2 and Nafion-H, employing the stirred method, was repeated at 140°C (Tables 32 and 33). In both cases the mass balance was higher than at 210°C, suggesting that fewer side reactions occur. The reaction was also para- selective in both cases. Thus, at both 140 and 210°C, the reaction is more para- selective over H-Nu-2 than over the non-porous Nafion-H. Of those Fries rearrangements of phenyl benzoate previously reported in the literature (Section 3.1.5, Table 14) few reactions were performed at either 140 or 210°C in the absence of solvent which are directly comparable. Over $AlCl_3$ or $TiCl_4$ the rearrangement is para- selective after 15 minutes. There is a prior report of rearrangement over Nafion-H at 150°C to yield a para/ortho ratio of 1.4 after 4h in the absence of solvent, compared to 2.1 after 4h in the present study. At 210°C, a prior example of catalysis by Nafion-H in nitrobenzene solvent

Table 31 Rearrangement of phenyl benzoate (sorption method, 210°C)

catalyst	T (°C)	time (h)	2-HBP	4-HBP	ph[a] (mol%)	pb[b]	p/o	total[c]
H-Nu-2	210	24	13.8	7.2	25.2	12.4	0.5	58.6
H-Nu-2 (dried)	210	24	14.1	4.7	26.5	15.1	0.3	60.4
H-ZSM-5 (H-Rblb)	210	24	3.4	0.5	11.7	61.1	0.2	76.7
H-EU-1	210	24	4.5	1.6	16.4	43.4	0.4	65.9

Table 32 Rearrangement of phenyl benzoate over H-Nu-2 (stirred, 140°C)

time (h)	T (°C)	2-HBP	4-HBP	ph	pb (mol%)	p/o	total
0.5	140	-	-	6.0	92.4	-	98.4
1		-	0.2	14.1	77.8	-	92.1
4		<0.1	1.2	18.3	70.7	-	>90.3
24		2.2	5.0	19.5	59.1	2.3	85.8
48		2.8	7.7	19.1	51.2	2.8	80.8
72		3.6	8.6	20.6	46.8	2.4	79.6

Table 33 Rearrangement of phenyl benzoate over Nafion-H (stirred, 140°C)

time (h)	T (°C)	2-HBP	4-HBP	ph	pb (mol%)	p/o	total
0.5	140	-	-	3.9	94.5	-	98.4
1		-	-	7.1	87.6	-	94.7
4		1.6	3.3	12.0	70.9	2.1	87.8
24		8.7	16.2	14.5	40.3	1.9	79.7
48		12.4	17.9	15.7	29.3	1.4	75.3
72		12.6	17.6	17.8	26.0	1.4	74.0

was para- selective after 12h. With $AlCl_3$ at 190°C the ortho-product predominates after 7h.

In those reactions over H-Nu-2 and Nafion-H at 210°C, the yield of 4-HBP appears to decline with time and over Nafion-H at 210°C, the yield of 2-HBP also decreases (Tables 28 and 30). There is no concomitant increase in the yield of the other isomer so this effect is unlikely to be attributed to para ⟶ ortho isomerism. It has been reported that the Fries rearrangement of aryl benzoates is an equilibrium process[119] with trifluoromethanesulphonic acid as catalyst, but in this case, the overall recovered yield of 2-HBP, 4-HBP and phenyl benzoate decreases. The aldol condensation, which was considered to be one route by which the phenolic products of the rearrangement of phenyl acetate could be consumed cannot occur in this case. Presumably, there are a number of side reactions, perhaps including decomposition leading to coke formation.

The benzoyl esters of 2-HBP and 4-HBP were not detected under the g.c. analysis conditions.

4. THE ALDOL CONDENSATION

4.1 Introduction

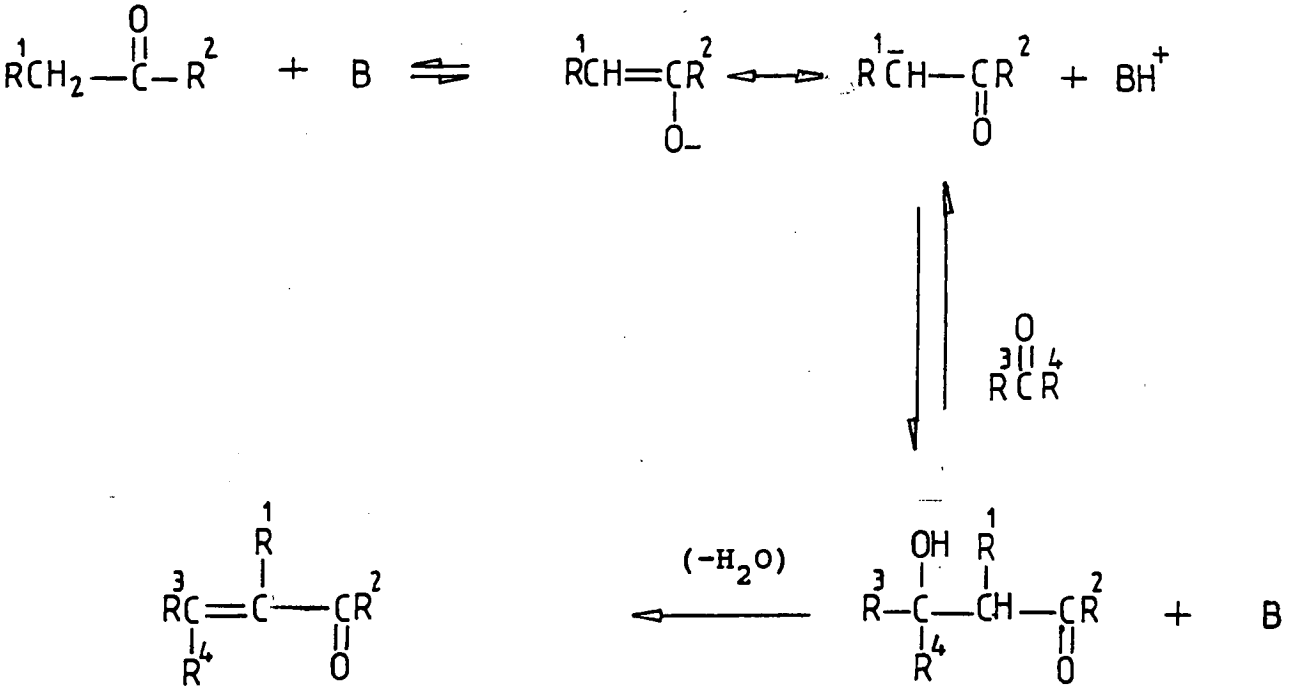
In Chapter 3, it was observed that both 4-hydroxyacetophenone [4-HAP (22)] and 4-acetoxyacetophenone (4-AAP (26)] were products of the rearrangement of phenyl acetate over zeolites. The yield of these products built up to a maximum and then declined when monitored with time. The effect was particularly marked over H-Nu-2 where unidentified, high molecular weight peaks were observed by g.c. (Table 26). In addition, when authentic samples of 4-HAP and 4-AAP were heated over H-Nu-2 low mass balances were detected by g.c.

It was postulated that these carbonyl compounds may undergo aldol condensation reactions as one pathway to contribute to their disappearance (Scheme 15). Water released in this process might contribute to the considerable phenol formation observed in zeolite-catalysed Fries rearrangement of phenyl acetate.

Some zeolite-promoted aldol reactions, mainly involving aliphatic carbonyl compounds have been reported previously.[23,24] Prior to the present work the only literature example of an aromatic aldol reaction was the self-condensation of acetophenone over the low silica, acidic zeolites H-Y and H-Mordenite.[141] An examination of aromatic aldol condensations over H-Nu-2 zeolite is discussed in this chapter.

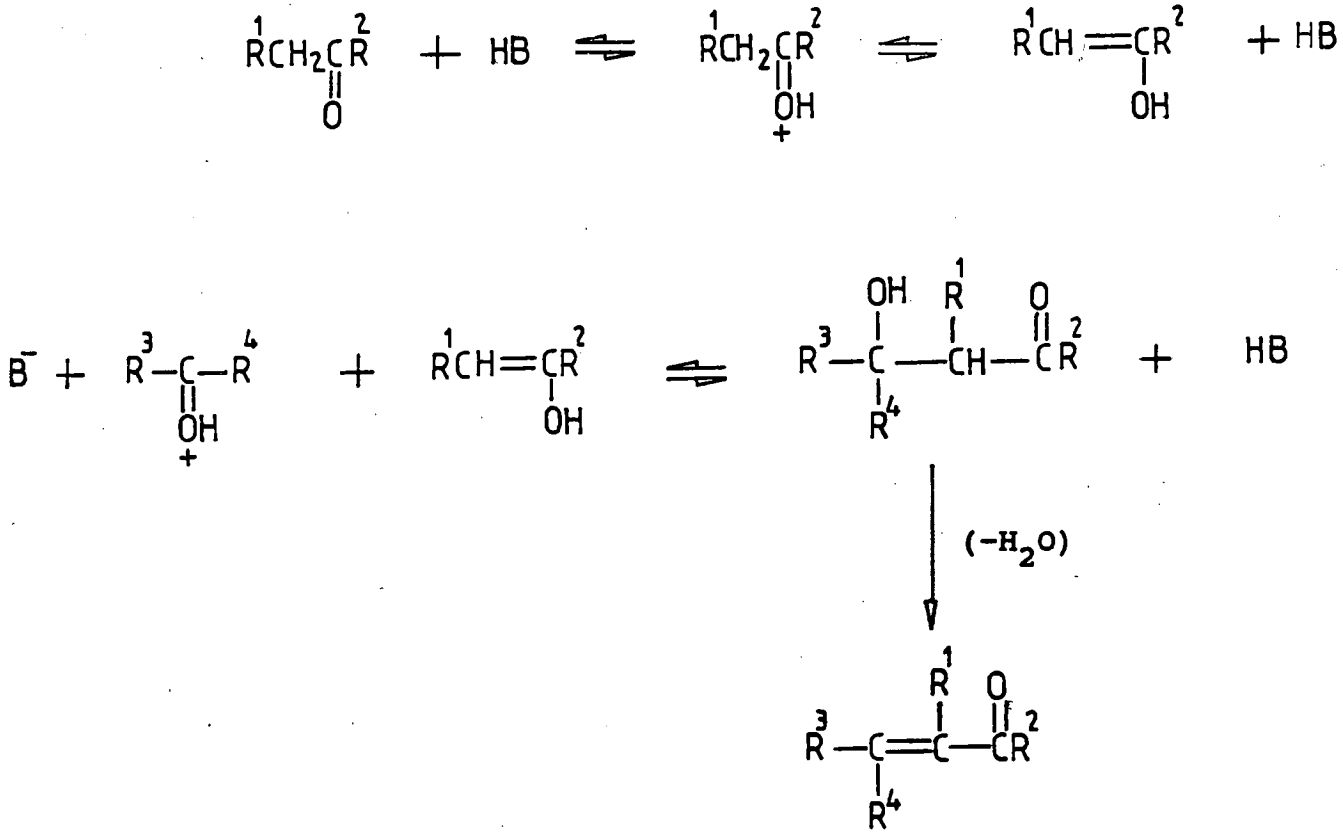
Scheme 17

Base catalysis of the aldol condensation



Scheme 18

Bronsted acid catalysis of the aldol condensation



4.1.1 Background

The aldol condensation reaction is the addition of the α-carbon of one aldehyde or ketone molecule to the carbonyl carbon of another molecule. The initial products, β-hydroxyaldehydes or ketones, usually dehydrate under the conditions of the reaction to afford α,β-unsaturated carbonyl compounds. The enormous importance of this reaction in synthetic organic chemistry has been demonstrated in an extensive review by Nielsen and Houlihan.[142]

While the aldol condensation is more commonly performed under basic conditions, acidic catalysts have also been widely employed. Typical basic catalysts are metal hydroxides and aluminium tert-butoxide. Acid catalysts include proton acids, eg. HCl and H_3PO_4, and Lewis acids such as BF_3, BCl_3 and $ZnCl_2$. Nielsen and Houlihan have tabulated known aldol condensations and the catalysts employed.

Five main categories of aldol reaction can be identified. These are: self-condensation of ketones, self-condensation of aldehydes, condensation between two different ketones, condensation between two different aldehydes and mixed condensation of an aldehyde and a ketone. The latter two categories are often termed the Claisen-Schmidt reaction.

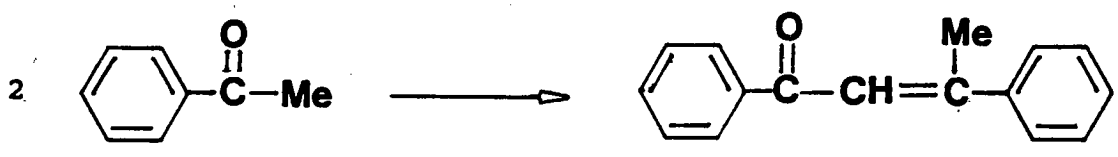
4.1.2 Mechanism

The mechanisms of both base- and acid-catalysed aldol condensations have been well-characterised and are discussed in detail in the review by Nielsen and Houlihan[142]. Their pathways are outlined in Schemes 17 and 18.

At least one of the reacting carbonyl components must contain a proton at the carbon α- to the carbonyl group to allow enolisation. Mechanistic studies have demonstrated that each step is an equilibrium process. Complicated reaction mixes can arise in the aldol condensation, as the α,β-unsaturated carbonyl products can undergo further condensation reactions with the starting material.

4.2 Results and Discussion

The self-condensation of acetophenone to yield β-methyl chalcone (27) has been widely reported in the literature.[142,143]



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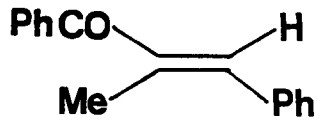
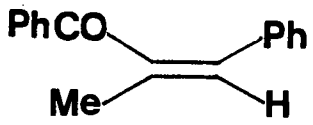




trans- ß-methylchalcone

cis- ß-methylchalcone

Ph = phenyl, Me = methyl.

The reaction has been catalysed by bases, eg. aluminium tert-butoxide,[144] Al_2O_3[145] and CaH_2,[146] and by acids, eg. HCl,[147] HBr,[148] $AlCl_3$,[149] PCl_5,[150] $ZnCl_2$,[151] SiO_2/Al_2O_3,[152] acidic clay[152] and acidic ion-exchange resin.[153] This system was chosen as a model reaction for the behaviour of 4-HAP and 4-AAP as both the starting material and product were readily available and characterised.

An authentic sample of ß-methylchalcone was synthesised from commercially available acetophenone with a *trans/cis* isomer ratio of 91:9. The ratio was determined by ^1H n.m.r. integration of the ß-methyl doublets of the two isomers at δ2.6 (*trans*) and δ 2.3 (*cis*). That the major isomer was the *trans*-isomer was confirmed by a Nuclear Overhauser Enhancement (NOE) difference experiment. Selective irradiation at the methyl signal (δ2.6) of the major isomer did not enhance the methine

signal at δ 7.2. However, irradiation at δ 2.3, the ß-methyl signal of the minor isomer enhanced the methyl signal at δ 6.7, indicating the spatial proximity of these groups and that the minor isomer had the *cis*-configuration.

Results for the self-condensation of acetophenone by H-Nu-2 are shown in Table 34. As discussed above, *trans/cis* isomer ratios were determined by ^{1}H n.m.r. integration of ß-methyl signals. In reactions 1-4, the product mixture was analysed by g.c.. In reaction 5, the ß-methylchalcone was separated from unreacted acetophenone and fully characterised.

Thus, self-condensation of acetophenone is catalysed by H-Nu-2 to afford yields of between 8-18% of ß-methylchalcone (based on starting acetophenone). In the absence of zeolite, under the same conditions as reaction 5, no ß-methylchalcone was detected. All of the reactions exhibited selectivity for the *trans*-isomer, consistent with previous reports on this reaction, where the stereoselectivity has been discussed.[145,154-156] Long reaction times appear to favour formation of the *cis*-isomer, demonstrated by comparison of reactions 1, 3 and 4. An increase in the amount of catalyst employed (reaction 3) also improved the relative proportion of *cis*-isomer.

Table 34 Self-condensation of acetophenone over H-Nu-2

reaction	acetophenone/ catalyst ratio (w/w)	T (^{o}C)	time (h)	recovered[e] acetophenone (mol %)	ß-methylchalcone[e] (mol %)	*trans/cis* ratio
1	4	120	18.5	68.7[a]	11.3[a]	95:5[b]
2	3	170	24	48.6[a]	8.8[a]	96:4[b]
3	2	120	89	67.2[a]	12.1[a]	77:23[b]
4[d]	4	120	72	58.4[a]	17.9[a]	80:20[b]
5[d]	4	120	48	56.2[c]	13.2[c]	90:10[b]

a determined by g.c.
b determined by n.m.r.
c isolated yield
d 4A mol. sieve in condenser
e mol % yield based on starting acetophenone

In all cases, the yields of β-methylchalcone were low. The position of equilibrium for the self-condensation of ketones lies towards the starting ketone,[143,157] so forcing conditions such as strongly acidic or basic catalysis or removal of the product as it is formed are usually required.

In an attempt to promote condensation by removal of water from the reaction mixture, 4A molecular sieve was placed in the condenser. However, as demonstrated by reactions 4 and 5, this measure did not lead to a marked improvement in the yield of β-methylchalcone.

At higher temperature, 170°, the reaction mixture appeared charred and the isolated products were discoloured (reaction 2). The low yield of β-methylchalcone suggests that polycondensation and/or coke formation in the zeolite had occurred. Indeed, the mass balance in each case is low (<100%) which may indicate that further reaction of β-methylchalcone takes place.

Thermal gravimetric analysis (t.g.a.) of the recovered zeolites indicated the extent of coke formation in each case by comparison with the weight loss of clean, unused H-Nu-2 (Table 35). Coke formation was significantly greater at higher temperature (reaction 2).

Table 35 t.g.a. analysis of recovered zeolite

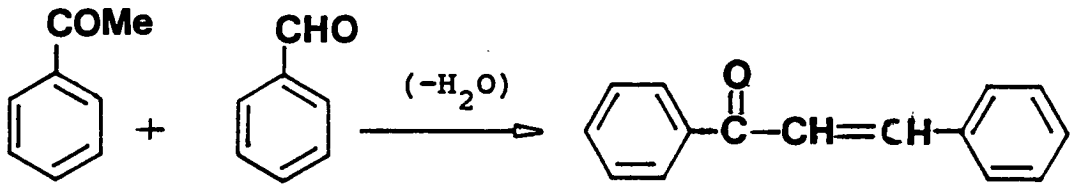
Reaction	% wt loss[a]
1	17.6
2	22.3
3	17.3
4	16.1
H-Nu-2	13.4

a = 0 - 900°c

The trimer, 1,3,5-triphenylbenzene has been reported as a by-product of the aldol condensation of acetophenone,[146,147,152,153] particularly in acid-catalysed processes. It was not detected in the product residues of the H-Nu-2 promoted reactions when analysed by mass spectrometry. This is not surprising as 1,3,5-triphenylbenzene is unlikely to fit inside the channel system of H-Nu-2.

The condensation of acetophenone with benzaldehyde has also been examined over H-Nu-2. This reaction is usually catalysed by bases such as NaOH[158] and NaOMe,[158,159] but is also promoted by HCl[158-160] and BF_3.[158,161]

Acetophenone and benzaldehyde were stirred with H-Nu-2 at 120° for 48 hours to afford a 75% yield of chalcone (28).



(28)

However, under the same conditions, but in the absence of zeolite, a 15% yield of chalcone was isolated. This reaction occurs more readily than the self-condensation of acetophenone as the aldehyde carbonyl group is more reactive to nucleophilic attack by the enolised ketone.[143,157]

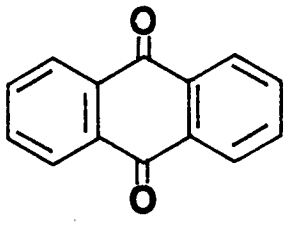
Despite this, the yield is considerably improved in the presence of H-Nu-2.

In conclusion, it has been demonstrated that the aldol self-condensation of acetophenone and the Claisen-Schmidt condensation of acetophenone and benzaldehyde are promoted by H-Nu-2 zeolite. The aldol reaction is therefore one potential pathway for the disappearance of 4-HAP and 4-AAP in the Fries rearrangement of phenyl acetate over zeolites.

5. ANTHRAQUINONE SYNTHESIS

5.1 Introduction

Anthraquinone [anthracene-9,10-dione (29)] is an important intermediate in the manufacture of anthraquinone dyes. It was first prepared synthetically by Laurent in 1835 by the oxidation of anthracene with nitric acid. Since then, the synthesis, characterisation and chemistry of anthraquinone and its derivatives has been investigated extensively.



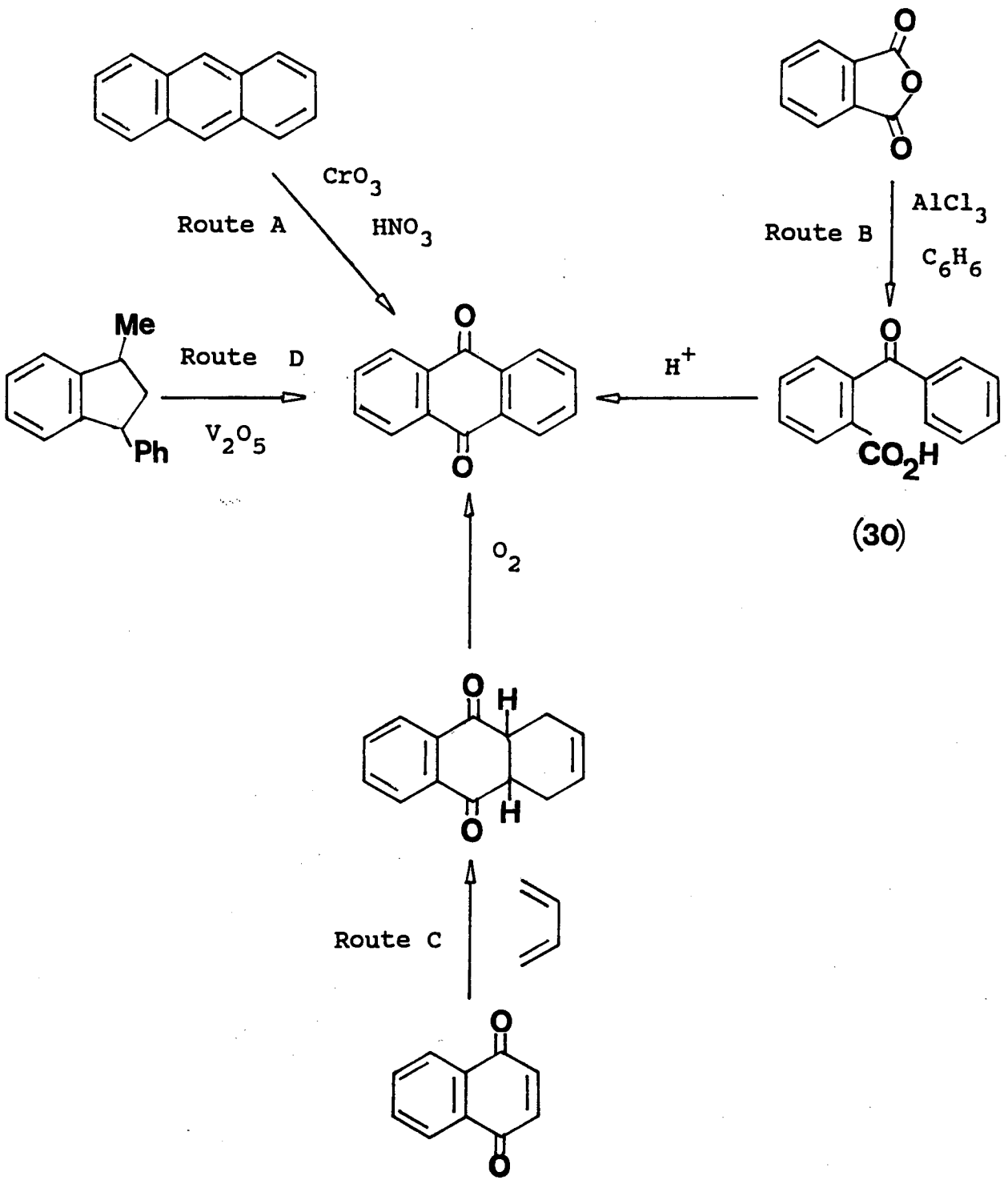
(29)

There are four major industrial processes for the synthesis of anthraquinone (Scheme 19). Of these, the oxidation of anthracene (route A) and the acid-catalysed cyclisation of 2-benzoylbenzoic acid, formed by the Friedel-Crafts reaction of phthalic anhydride and benzene (route B), are predominant.

Oxidation of anthracene is usually performed on an industrial scale by chromic acid[164] or nitric acid.[165] Catalytic oxidation of anthracene has been reported over silver and ceric salts[166] and in the vapour phase over catalysts containing vanadium pentoxide.[167,168,169]

Route C describes the preparation of anthraquinone from the Diels-Alder reaction of 1,4 naphthoquinone and 1,3-butadiene. The resultant tetrahydroanthraquinone is oxidised in air in the presence of base to yield anthraquinone.[170,171] If the process is conducted in nitrobenzene solution, anthraquinone can be obtained directly without isolation of the tetrahydroanthraquinone intermediate.

Scheme 19 Industrial Synthesis of Anthraquinone



The synthesis can also be achieved directly from naphthalene by oxidation to 1,4-naphthoquinone, followed by Diels-Alder reaction with 1,3-butadiene.[172,173] In addition, the Diels-Alder reaction of benzoquinone with two molar equivalents of butadiene also yields anthraquinone *via* octahydroanthraquinone, followed by oxidation.[174,175]

The most recently developed route to anthraquinone is the oxidation of 1-methyl-3-phenylindane and its derivatives (route D). This process has been achieved over catalysts which contain vanadium pentoxide.[176,177] The dimerisation of styrene readily affords 1-methyl-3-phenylindane.

Of particular interest to the present study of reactions over zeolites is route B, cyclisation of 2-benzoylbenzoic acid [2-BBA (30)] to anthraquinone. Cyclisation proceeds readily in concentrated sulphuric acid or weak oleum at temperatures usually between 90-150^{o}C.[177,180] While sulphuric acid is the usual catalyst, P_2O_5,[181] polyphosphoric acid,[182,183] SO_3,[184] solid mixed oxide catalysts such as SiO_2-Al_2O_3[185] and SiO_2-Al_2O_3-Fe_2O_3-MgO-CaO,[186] activated clay[187] and Nafion-H perfluorinated cation-exchange resins[188] have also been reported to promote this cyclisation. Temperatures up to 400^{o}C were utilised for cyclisations over the solid mixed oxide catalysts.

It was therefore considered that acid zeolites might be suitable catalysts for this reaction, employing both the zeolite acidic sites and the steric restrictions imposed by the channels to promote cyclisation and with the advantage that the catalysts could be regenerated and re-used.

The Lewis acid, aluminium chloride,[189-191] is the usual catalyst for the Friedel-Crafts reaction of phthalic anhydride and benzene to give 2-BBA, although $HF-BF_3$[192] has also been used. It was thus considered feasible that zeolites might also catalyse this stage of the process with direct "in situ" cyclisation of the 2-BBA formed to anthraquinone. In Chapter 3 it was demonstrated that zeolites can effect reactions which are promoted by Lewis acids.

Prior to this study, there were a number of reports of high temperature, vapour phase reaction of phthalic anhydride and benzene over solid acid catalysts to yield anthraquinone directly. The catalysts are mainly metal oxides and mixed oxides, e.g. $SiO_2-Al_2O_3$,[193,194] TiO_2, SnO_2,[195,196] $SiO_2-Al_2O_3-B_2O_3$, TiO_2, ZrO_2, Al_2O_3, WO_3, SnO_2, PbO,[198] and $SiO_2-Al_2O_3-Fe_2O_3$[199].

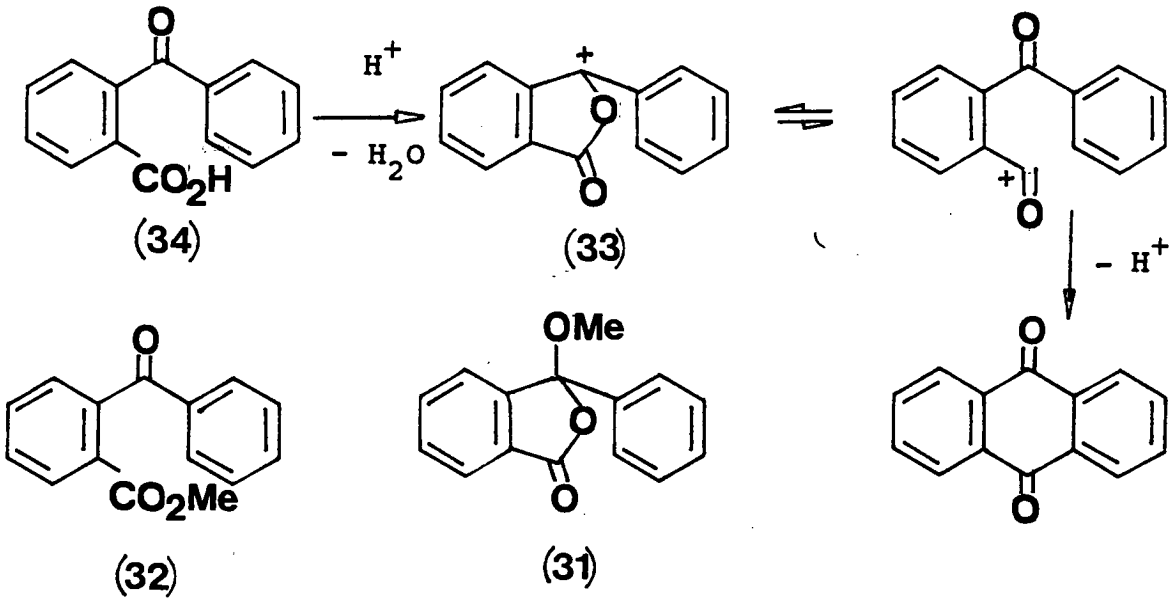
In addition, there are two examples of direct conversion of phthalic anhydride and benzene to anthraquinone over zeolites. The materials employed were a cerium (III) exchanged zeolite[200] at 550°C and Na-X.[201] However, as discussed in Chapter 1,

these high temperature vapour phase reactions are outwith the scope of the present investigation.

5.1.1 Mechanism of the cyclisation of 2-benzoylbenzoic acid to anthraquinone

The accepted mechanism for the ring closure of 2-benzoylbenzoic acid (2-BBA) to anthraquinone was first proposed by Newman[202] for the cyclisation in sulphuric acid (Scheme 20).

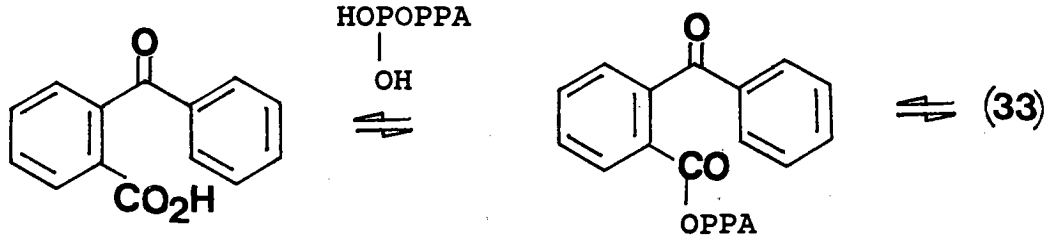
Scheme 20



Newman showed that when a cold solution of 2-BBA in 98% sulphuric acid was poured into methanol, the pseudo methyl ester (31) was the major product. The pseudo ester rearranged to the normal ester (32) in sulphuric acid. Newman noted that sulphuric acid solutions of 2-BBA require heat to cyclise to anthraquinone and postulated that the cyclic ion (33) cleaves to the open chain acyl ion on heating, which can rotate into position for ring closure.

Downing and Pearson have concluded that a similar mechanism operates in polyphosphoric acid. In sulphuric acid, the dehydration step (34) to (33) is believed to take place by simple protonation and elimination of water. In polyphosphoric acid, this step was considered to be the result of reaction of the hydroxyl group of 2-BBA with an anhydride linkage of the polyphosphoric acid to give a mixed anhydride (Scheme 21). This can then cleave to the carbonium ion, the driving force being the formation of the resonance-stabilised polyphosphate anion (OPPA).

Scheme 21



The presence of the cyclic ion (33) in sulphuric acid solution was further demonstrated by Ross and Schwarz. When 2-BBA in sulphuric acid was treated with benzene, toluene or t-butylbenzene, the products were 3,3—diphenylphthalide, 3-phenyl-3-p-tolylphthalide and 3-phenyl-3-(p-t-butylphenyl-phthalide) respectively.

Newman[202] has noted the ease with which this intramolecular acylation takes place ortho to the ketone. Ketones do not normally undergo Friedel-Crafts acylation at the ortho-position, being deactivating and meta-directing.

In polyphosphoric acid, Downing and Pearson measured the rate of formation of anthraquinone from 2-aroylbenzoic acids. They noted that the rate reaches a maximum in polyphosphoric acid (about 80% of P_2O_5 content) and that under these conditions, 2-BBA reacts about five times more rapidly than 2-(4-methylbenzoyl)benzoic acid and about 70 times more rapidly than 2-(4-chlorobenzoyl)benzoic acid. Similarly, Noyce and Kittle[204] compared the rates of formation of anthraquinones from benzoylbenzoic acids substituted in the benzoyl ring. In 99-100% H_2SO_4, 2-benzoylbenzoic acid cyclised approximately four times faster than 2-(4-methylbenzoyl) benzoic acid. As the methyl group in the benzoyl ring would have a greater stabilising effect on the cyclic carbonium ion than the open-chain acyl ion, this observation was taken as further evidence of a cyclic carbonium ion intermediate.

5.2 Results and Discussion

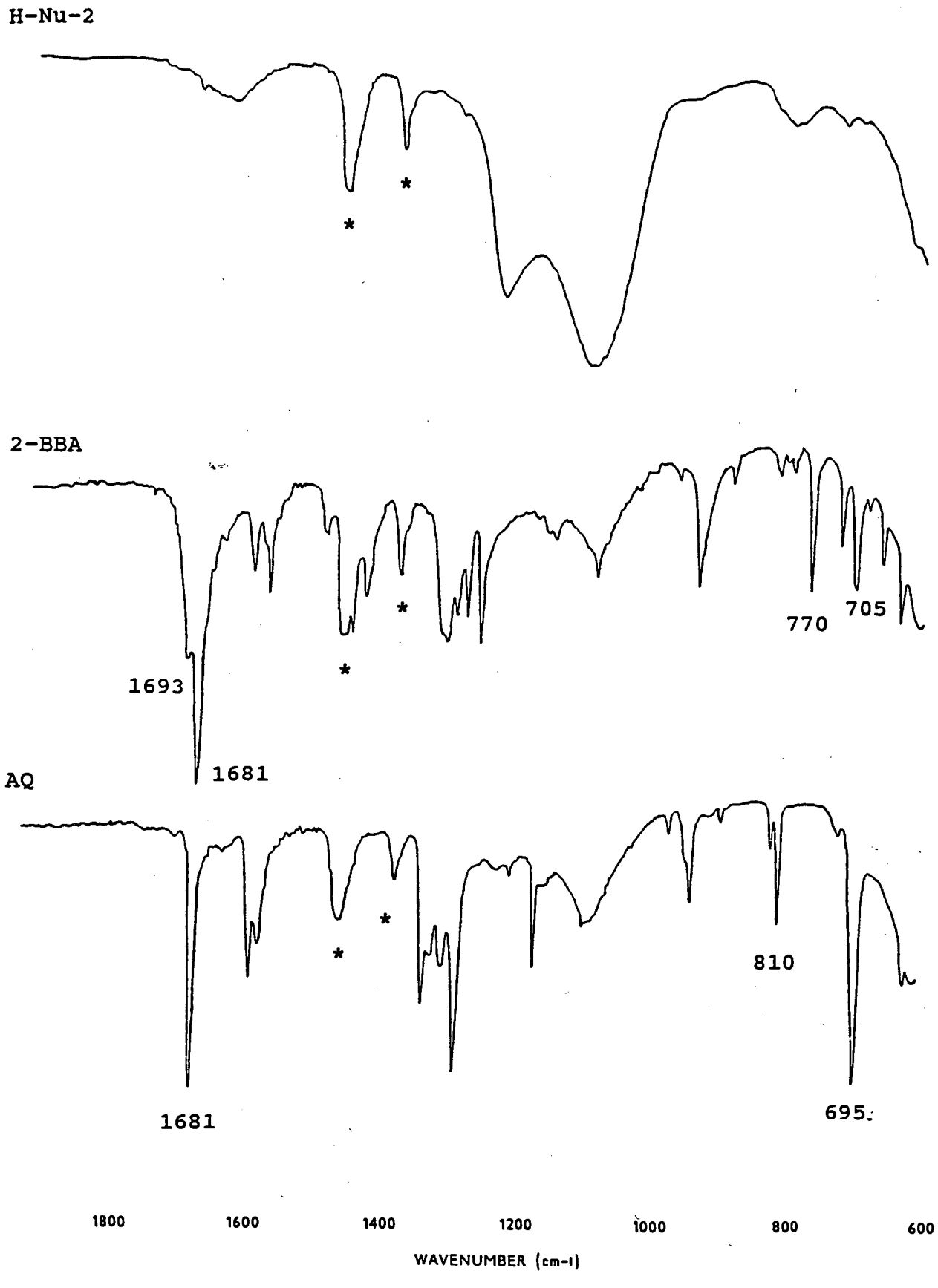
The intramolecular cyclisation of 2-benzoylbenzoic acid [2-BBA (30)] to anthraquinone [AQ (29)] was examined in the presence of zeolites. As AQ is only sparingly soluble in most organic solvents, it was not considered feasible to perform the reaction in solution. A series of reactions were performed by

sorption of 2-BBA onto the zeolite. A similar procedure has previously been employed for the photolysis of dibenzyl ketones.[28] A solution of 2-BBA in methylene chloride was mixed with a preweighed quantity of zeolite and the solvent removed under vacuum to leave a dry powder. This method was employed to maximise sorption of 2-BBA into the zeolite channels. In all the reactions described, a 2:3 w/w ratio of 2-BBA to zeolite was used, far more than can be accommodated within the channels. The progress of the cyclisations was monitored by infra-red (i.r.) spectroscopy.

Batches of starting material (2-BBA) and zeolite were prepared by the above procedure and divided into portions, thus ensuring a constant composition throughout. The portions were placed in a heating block maintained at constant temperature and successively removed after heating for the required time. After cooling, the i.r. spectrum (nujol mull) of the whole sample (including the zeolite) was recorded. Conversion to AQ was determined by the disappearance of characteristic bands of 2-BBA and the appearance of characteristic AQ peaks.

The i.r. spectrum of H-Nu-2 was recorded between 1800 and 600 cm^{-1} (Figure 19). It shows a strong absorption between 1300 and 900 cm^{-1}. The other zeolites included in this study (H-ZSM-5, H-Mordenite and H-Nu-10) also show strong absorptions in this region. The spectra of AQ and 2-BBA (Figure 19) exhibit strong bands outwith the broad region of zeolite absorption which were chosen to monitor the reaction. AQ has a

Figure 19 I.r. spectra (nujol mull) of H-Nu-2, 2-BBA and anthraquinone between 1800 cm^{-1} and 600 cm^{-1}.



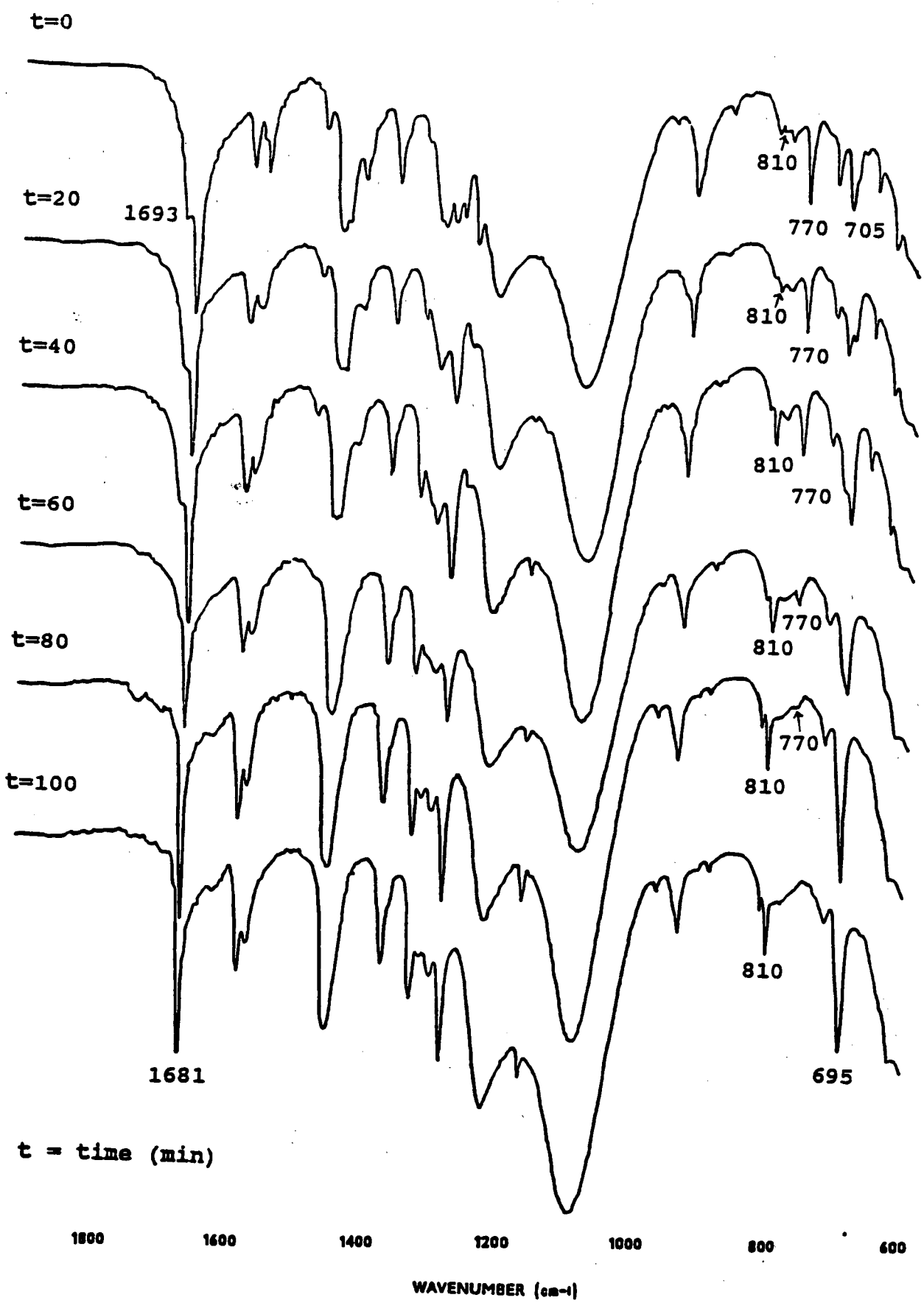
* = peak attributed to nujol.

single carbonyl peak at 1681 cm^{-1} whereas 2-BBA exhibits a strong carbonyl peak at 1681 cm^{-1} with a shoulder at 1693 cm^{-1}. The spectrum of AQ also shows strong bands at 810 and 695 cm^{-1} which do not coincide with peaks in the spectrum of 2-BBA. These peaks have been identified as C-H out of plane bending bands.[206] In addition to the changes in the carbonyl region the cyclisation was also monitored by the appearance of these C-H peaks and the subsequent disappearance of peaks at 770 cm^{-1} and 705 cm^{-1} in the starting material.

An example of this method is shown in Figure 20. Samples of 2-BBA sorbed onto the H-Nu-2 were heated at 200°C. The i.r. spectra of the starting material and successive samples at 20 minute intervals wre recorded. Bands assigned to AQ were observed, e.g. after 40 minutes a sharp peak at 810 cm^{-1} was present, indicating some conversion to AQ, although the carbonyl peak at 1681 cm^{-1} still exhibited a shoulder at 1693 cm^{-1} attributed to 2-BBA. The reaction was considered to be complete after 100 minutes (Table 36). None of the characteristic 2-BBA peaks remained and a single carbonyl peak and strong bands at 810 cm^{-1} and 695 cm^{-1} were observed. Note that slight variations in the peak sizes between samples are due to differences in sample size and consistency.

The same procedure was repeated over H-Nu-2 at 170°C and over H-ZSM-5 (H-Rblb), H-Nu-10 (WX149CX) and H-Mordenite at 200°C. The extent of conversion to AQ was estimated from the i.r. spectra of authentic samples of 2-BBA and AQ sorbed onto H-Nu-2

Figure 20 Conversion of 2-BBA to AQ over H-Nu-2 monitored by i.r.



in the following molar ratios: 100:0, 95:5, 90:10, 70:30, 50:50, 30:70, 10:90, 5:95, 0:100. In those standard samples which contained only 5% of either component the minor constituent could not be clearly detected in the i.r. spectrum. Estimated conversions from comparison with these standard samples were therefore only recorded after at least 10% conversion had taken place.

Thus, 2-BBA cyclised over H-Nu-2 to yield 25% AQ after 180 minutes at 170°C (Table 36). At 200°C the rate was substantially increased and i.r. indicated complete ring closure to AQ after 100 minutes. Much lower conversions were achieved over H-ZSM-5 (30%), H-Nu-10 (85%) and H-Mordenite (50%) after 62, 20 and 20 hours respectively. In similar reactions in the absence of zeolite and over non-acidic Na-Y, no AQ was detected after 20 hours.

The ring closure is therefore performed most efficiently over H-Nu-2. 2-BBA is likely to be readily sorbed into the channels of H-Nu-2 but not by H-ZSM-5 or H-Nu-10 (Section 1.1, Table 1). The slow conversions over H-ZSM-5 and H-Nu-10 probably occur on the zeolite external surface. The higher conversion over H-Nu-10 may be attributed to the high surface area of this sample. It consists of very fine particles (Section 6.2.8) and occupies a significantly larger volume for weight than the other zeolites employed in this study. The low conversion over H-Mordenite is probably because the channels are blocked, a

Table 36 Estimated conversion of 2-BBA to AQ over zeolites

zeolite	H-Nu-2		H-Nu-2 (dried)		H-Nu-10 (WX149CX)		H-ZSu-5 (H-Rb1b)		H-Mordenite	
temp °C	time (min)	AQ (mol%)	time (min)	AQ (mol%)	time[a] (min)	AQ (mol%)	time[a] (min)	AQ (mol%)	time[a] (min)	AQ (mol%)
200	0	-[b]	0	-[b]	0	-[b]	0	-[b]	0	-[b]
	20	10	20	40	20	-[b]	20	-[b]	20	-[b]
	40	40	40	85	60	-[b]	60	-[b]	40	-[b]
	60	85	60	90	100	-[b]	100	-[b]	60	-[b]
	80	90	80	100	160	10	18h	20	120	-[b]
	100	100	100	100	18h	70	65h	30	180	-[b]
	120	100			20h	85			20h	50
170	0	-[b]								
	20	-[b]								
	40	-[b]								
	60	-[b]								
	80	-[b]								
	100	10								
	120	15								
	150	20								
	180	25								

a - time in minutes except where indicated

b - not detected (detection limit 10%)

common fault in Mordenites, as the channel size is only slightly smaller than H-Nu-2.

To investigate the effect of sorbed water in the zeolite channels, the reaction was repeated under dry conditions over H-Nu-2 at 200°C. A small but significant rate enhancement was indicated by i.r. After 80 minutes with dried zeolite the conversion was complete compared with 90% completion with the untreated sample. As the ring closure is a dehydration process, the dry zeolite is likely to be quickly deactivated by water produced during the reaction.

The product AQ could be efficiently removed from the zeolite by extraction or sublimation. 2-BBA sorbed onto H-Nu-2 (undried) in a 2:3 w/w ratio was heated at 200°C for two hours. Continuous extraction gave a 93% yield of crude AQ. The pure product was isolated in 77% yield by sublimation. AQ could also be sublimed directly from 2-BBA sorbed onto H-Nu-2. Thus, when a sample was heated at 270°C, the ring closure and isolation of AQ was achieved in one step. Pure AQ was sublimed from the sample in 79% yield, after 10h.

In all these reactions, the 2-BBA and the zeolite were employed in a 2:3 w/w ratio. Thermal gravimetric analysis (t.g.a.) of H-Nu-2 allowed to equilibrate in air showed the maximum water uptake of H-Nu-2 to be 13.4% by weight. This figure may be used as an approximate estimate of the maximum limit for sorption of 2-BBA. If 2g of 2-BBA were sorbed onto 3g of H-Nu-

2, the maximum weight of 2-BBA taken up into the zeolite channels would be 0.27g. However, all of the 2-BBA was converted into AQ therefore it can be concluded that the reaction is catalytic.

After extraction of AQ, the H-Nu-2 zeolite was grey. After heating overnight at 550°C, the clean white zeolite was regenerated. When this sample was re-used at 200°C by the method previously described, a further 90% yield of crude anthraquinone was isolated by extraction.

As the cyclisation of 2-BBA can be catalysed by H-Nu-2, direct synthesis of AQ from phthalic anhydride and benzene was also attempted over H-Nu-2. However, when phthalic anhydride was sorbed onto H-Nu-2 and refluxed in benzene for five hours there was no evidence for the formation of either 2-BBA or AQ and a quantitative yield of phthalic anhydride was recovered. In a similar reaction, a solution of phthalic anhydride in benzene was refluxed with H-Nu-2 for 8.5 hours. As before, neither 2-BBA or AQ were detected and the product appeared to be a mixture of phthalic anhydride and phthalic acid. These liquid phase reactions were limited by the relatively low boiling point of benzene.

H-Nu-2 is therefore an efficient, re-usable catalyst for the cyclisation of 2-BBA to AQ. However, higher reaction temperatures (200°C) are required than those normally employed when the reaction is performed in sulphuric acid (90-150°C).

The progress of the cylcisation can be effectively monitored by i.r. Of interest for further work in this area would be shape-selective cyclisations catalysed by zeolites, eg. 2-(3-methylbenzoyl)benzoic acid can cyclise to both 1-methyl- and 2-methylanthraquinone. Reaction in a zeolite may yield one of the products selectively.

6. EXPERIMENTAL - ZEOLITE SYNTHESIS AND PREPARATION

6.1 Instrumentation and analysis

i) X-ray diffraction (x.r.d.):

X.r.d. patterns were recorded on a Philips Powder X-ray Diffractometer with fine-focus copper X-ray tube at 1^{o} 20/min and range 4×10^{3}, time constant 2 and chart rate 1cm/min.

ii) Inorganic analysis (a.a.s.):

Inorganic analysis (atomic absorption spectroscopy) was kindly supplied by Dr. J. Casci of ICI Chemicals and Polymers Limited, except where indicated.

iii) Scanning electron microscopy (s.e.m.):

S.e.m. was kindly supplied by Dr. J. Casci.

iv) Thermal analysis (t.g.a., d.t.g., d.t.a.):

Thermogravimetric analysis (t.g.a.), differential thermal analysis (d.t.a.) and differential thermal gravimetry (d.t.g.) were recorded on a Stanton-Redcroft Simultaneous Thermal Analyser STA-780 between 20-900^{o}C in air.

6.2 Synthesis and Characterisation of zeolites

6.2.1 (Na,H)-EU-1

This zeolite was synthesised according to reference 13, with the gel composition:

$10Na_2O.Al_2O_3.60SiO_2.10HEXBr_2.3000\ H_2O$

10.33g NaOH (AnalaR, from BDH)

0.69g aluminium wire (AnalaR, from BDH)

46.52g SiO_2 (Cab-O-Sil M5, from BDH)

46.74g $HEXBr_2$ (hexamethonium bromide, pure grade from Fluka)

697.80g distilled water

The aluminium wire was cut into 1cm pieces and added to a solution of the NaOH in 11.07g water. This mixture was boiled until the aluminium had dissolved, topping up with water to maintain the volume. A solution of the hexamethonium bromide in 670.66g water was prepared, into which the silica was stirred. The aluminium solution was allowed to cool to room temperature and poured into the silica slurry. Water was added to make up the required amount. The gel was mixed with a hand blender for 5 minutes and transferred to an autoclave. It was heated at 170°C (with stirring, 150rpm) at autogeneous pressure for 68h. The product was filtered, washed thoroughly with water and dried overnight at 120°C to give 30.77g of "as made" (Na,HEX)-EU-1. The zeolite was calcined at 450°C for 48h to yield (Na,H)-EU-1.

x.r.d.: Confirmed EU-1 structure, no impurities detected.

a.a.s.:

Na	Al	Si (%w/w)	Si/Al ratio
0.19	1.65	35.9	20.9

Unit cell composition:

$Na_{0.69}$ $H_{4.42}$ $Al_{5.11}$ $Si_{106.88}$ O_{224}

s.e.m.: (Figure 21 Consisted of rounded/elliptical platelets. These discs possess fine structure on the surface and intergrow randomly to form loose aggregates.

"Discs" 0.5 - 3.0μm length
0.35 - 2.25μm width
0.17μm approx. depth

6.2.2 H-EU-1

This zeolite was prepared by ion-exchange of (Na,H)-EU-1 (Section 6.2.1). Ion-exchange was performed with 3.6ml of 1M HCl per gram of zeolite at 25°C for 1h. The product was washed thoroughly with water, dried at 120°C for 16h and activated at 450°C for 6h.

x.r.d.: Confirmed EU-1 structure intact.

a.a.s.:

Na	Al	Si (%w/w)	Si/Al ratio
0.02	1.65	37.6	21.9

There was a slight loss of aluminium on treatment with acid.

Unit cell composition:

$Na_{0.07}$ $H_{4.82}$ $Al_{4.89}$ $Si_{107.11}$ O_{224}

s.e.m.: H-EU-1 has a very similar morphology to (Na,H)-EU-1

(Section 6.2.1).

Particle size: 0.4 - 3.5μm length
0.3 - 2.25μm width
approx. 0.2μm depth

6.2.3 H-ZSM-5 (SKH-Z1, SKH-Z2, SKH-Z3, SKH-Z4)

These zeolites were prepared from Na-free reaction mixture compositions and therefore did not require the usual post-calcination step of acid exchange to yield the acid form of the zeolite. The synthesis procedure has been described in detail in reference.[207]

A series of zeolite reaction mixtures were prepared with gel compositions:

10 piperazine 2TPABr x[$Al(NO_3)_3$] 20 SiO_2 1000 H_2O

piperazine hexahydrate (PIPZ $6H_2O$) - from Aldrich (98%)

tetrapropyl ammonium bromide (TPABr) - from Aldrich

aluminium nitrate [$Al(NO_3).9H_2O$] - AnalaR, from BDH

SiO_2 -Cab-O-Sil M5, from BDH

distilled water

The value of x was chosen to give Si/Al ratios of 40, 60, 80 and 100 in the reaction mixtures. Each mixture weighed 400g. Crystallisations were performed at 95°C in polypropylene bottles in a thermostat bath, and were monitored by optical microscopy and x.r.d. When crystallisation was complete, the product was filtered at 95°C, washed with distilled water and dried at 110°C for 16h.

Reaction mixture compositions and crystallisation times which yielded the "as made" products are shown in Table 37.

Table 37

product "as made"	prod.mix Si/Al ratio	SiO_2 (g)	$Al(NO_3)_3$ $9H_2O$(g)	PIPZ. $6H_2O$(g)	TPABr (g)	H_2O (g)	cryst. time (days)
SKH-Z2	40	23.21	3.63	37.50	10.28	325.39	27
SKH-Z1	60	23.24	2.42	37.56	10.31	327.48	27
SKH-Z3	80	23.27	1.82	37.60	10.31	327.03	22
SKH-Z4	100	23.30	1.46	37.62	10.31	327.39	34

x.r.d: Confirmed the ZSM-5 structure for each of the above "as made zeolites.

Calcination at 550°C for 16h, then 800°C for 1h gave the acid products SKH-Z1 to SKH-Z4 used in this study. The zeolites were characterised by x.r.d., s.e.m. and a.a.s.

x.r.d: Confirmed the ZSM-5 structure for each of the calcined products.

a.a.s:	Na	Al	Si (%w/w)	Si/Al ratio
SKH-Z2	<0.002	0.97	43.2	42.8
SKH-Z1	<0.002	0.68	45.5	64.3
SKH-Z3	<0.002	0.53	41.1	74.5
SKH-Z4	0.003	0.35	41.9	115.0

Unit cell compositions:

SKH-Z2	$Na_{<0.005}$	$H_{2.19}$	$Al_{2.19}$	$Si_{93.81}$	O_{192}
SKH-Z1	$Na_{<0.005}$	$H_{1.47}$	$Al_{1.47}$	$Si_{94.73}$	O_{192}
SKH-Z3	$Na_{<0.006}$	$H_{1.27}$	$Al_{1.27}$	$Si_{94.73}$	O_{192}
SKH-Z4	$Na_{<0.008}$	$H_{0.82}$	$Al_{0.83}$	$Si_{95.17}$	O_{192}

s.e.m.:

SKH-Z2 Figure 22: This zeolite exhibited rectangular/ cuboid platelet morphology with slightly rounded end facets. The cuboid surfaces were mostly smooth with a small amount of twinning on basal planes. Fine secondary particulate material was observed adhering to surfaces. There was little evidence of intergrowth. Aggregates of up to 400μm were observed, but most of the particles were present as loose material.

Particle size: 2.0 - 6.5μm length
1.7 - 5.0μm width
approx. 1μm depth

SKH-Z1 Figure 23: As above, this zeolite also exhibited rectangular/cuboid platelet morphology with rounded end facets. Compared to SKH-Z2, twinning was more evident on basal planes. Again, a fine secondary particulate material was observed adhering to most surfaces. There was some intergrowth to form aggregates of up to 600μm, although much loose material was also present.

Particle size: 2.3 - 7.0μm length
1.5 - 5.0μm width
approx. 1μm depth

SKH-Z3 Figure 24: The morphology was similar to that of SKH-Z1 and 2, with fine secondary particulate material on cuboid surfaces. Surfaces were mostly smooth with a small amount of twinning on basal planes. Little intergrowth was observed. Particles did form aggregates of up to 600μm but most was present as base material.

Particle size: 3.5 - 6.3μm length
2.3 - 5.0μm width
approx. 1μm depth

SKH-Z4 Figure 25: The same rectangular/cuboid platelet morphology of samples 1-3 was observed. Twinning was evident on basal planes. Again, fine secondary particulate material was present. Intergrowth was limited, although aggregates of up to 400μm were present.

Particle size: 0.5 - 11.0μm length
0.3 - 5.0μm width
approx. 2μm depth

6.2.4 (Na,H)-ZSM-5 (Rb1b)

This sample was supplied in the "as made" form by Mr R Brown. It had been prepared by the method described in reference 6 from the gel composition:

$10Na_2O.\ Al_2O_3.\ 60\ SiO_2.\ 10$ HEXDL. $3000\ H_2O$

HEXDL - 1,6 hexanediol

The zeolite was calcined at 500°C for 16h before use.

x.r.d.: confirmed the ZSM-5 structure

6.2.5 H-ZSM-5 (H-Rb1b)

Acid exchange of (Na,H)-ZSM-5 (Section 6.2.4) gave H-ZSM-5. Exchange was performed at room temperature with 20ml of 0.1M HCl per gram of zeolite. The process was repeated three times, the product dried at 110°C and activated at 475°C for 16h.

x.r.d: Confirmed the ZSM-5 structure

a.a.s.:

Na	Al	Si	(%w/w)	Si/Al ratio
0.024	1.79	37.8		20.3

Unit cell composition:

$Na_{0.07}\ H_{4.44}\ Al_{4.51}\ Si_{91.49}\ O_{192}$

s.e.m.: Figure 26 The zeolite consists of ellipsoidal particles with both smooth and uneven surfaces. There was some evidence of intergrowth and aggregate formations of about 40μm.

Particle size: typically -

2.3 - 4.0μm length

1.0 - 1.8μm width

1.0 - 1.4μm depth

6.2.6 H-Nu-2 (H-ZP-280)

Supplied in the calcined, acid form by Dr J L Casci of ICI Chemicals and Polymers Limited.

x.r.d.: Indicated a highly crystalline Nu-2 type structure.

a.a.s.:

Na	Al	Si	(%w/w)	Si/Al ratio
<0.002	2.34	32.1		26.4

s.e.m.: Figure 27 Consists of elliptical/spherical platelets with uneven surfaces. Some aggregates up to 70μm were observed.

Particle size: typically 0.2 - 1.2μm length, width.

6.2.7 (Na,H)-Nu-10 (WZ 285)

Supplied in the "as made" form by Dr A Stewart of ICI Chemicals and Polymers Limited. The sample was about 90% pure with some amorphous material and a small amount of α-cristobalite. It was subsequently calcined at 500°C for 64.5h.

a.a.s:

Na	Al	Si	(%w/w)	Si/Al ratio
0.57	0.89	40.4		43.6

Unit cell composition:

$Na_{0.40}$ $H_{0.134}$ $Al_{0.54}$ $Si_{23.46}$ O_{48}

s.e.m.: Figure 28 Showed needle-like morphology. The needles intergrow/densely pack to form spherical aggregates 4.2 - 11.2μm in size. These aggregates in twin form agglomerates up to 1100μm in size. Loose needles were sometimes observed.

Needle size - 1.15μm typical length, up to 3.38μm 0.09μm diameter.

6.2.8 H-Nu-10 (WX 149 CX)

Supplied in the calcined, acid form by Dr A Stewart.

x.r.d.: Indicated Nu-10 type structure and trace impurity.

Inorganic analysis: Supplied by Dr. A. Stewart.

Na	Al	Si	(%w/w)	Si/Al ratio
0.0005	0.73	41.4		54.4

Unit cell composition:

$Na_{0.0003}$ $H_{0.43}$ $Al_{0.43}$ $Si_{23.57}$ O_{48}

s.e.m.: Figure 29 Indicated the co-existence of both needles and spherical particles. Needles start to appear on aggregates above 3um in size. Larger aggregates mostly consist of needles packing densely inside and the spherical particles being randomly dispersed outside.

Particle size: Spheres 0.08 - 0.88μm

Needles 0.90μm typical length

0.07 - 0.14μm diameter

6.2.9 (Na,H)-Nu-10 (AA53)

This sample was synthesised by Dr. A. Araya. The method and characterisation have been detailed previously[10]. Si/Al ratio of the product was 60. The "as made" material was calcined at 550°C for 72h.

6.2.10 H-Mordenite (TS2 600 HOA)

A commercial sample supplied by Dr J L Casci.

Si/Al ratio = 5.

6.2.11 (Cu(II),H)-Y

Prepared by ion-exchange of NH_4-Y (from Strem Chemicals Inc) with 0.2M $CuSO_4.5H_2O$ (20ml per gram of zeolite). The ion-exchange process was repeated three times and the product dried overnight at 95°C to give a pale blue powder.

x.r.d: Confirmed the Y-type structure was intact.

a.a.s.:	Na	Al	Si	Cu	(%w/w)	Si/Al ratio
	1.07	7.64	23.8	5.41		3.0

Unit cell composition:

$Na_{7.90}$ $Cu_{14.45}$ $H_{11.26}$ $Al_{48.08}$ $Si_{143.92}$ O_{384}

s.e.m.: Zeolite did not appear to possess any well-defined morphology. It was composed of small, irregular structures which aggregated together.

Particle size 0.1 - 1.5μm.

6.2.12 Na-A

A commercial sample obtained from BDH (4A mol.sieve) in powdered form.

6.2.13 Na-Y

A commercial sample obtained from Strem Chem. Inc. in powdered form.

6.2.14 $AlPO_4$-5 aluminophosphate molecular sieve

Supplied by Dr. C.D. Williams (Edinburgh University).

6.2.15 General preparation of zeolites for organic reactions

All zeolites and molecular sieves were employed in powdered form. Except where indicated in the text, zeolites were allowed to equilibrate in air for at least 1 hour before use.

Figure 21

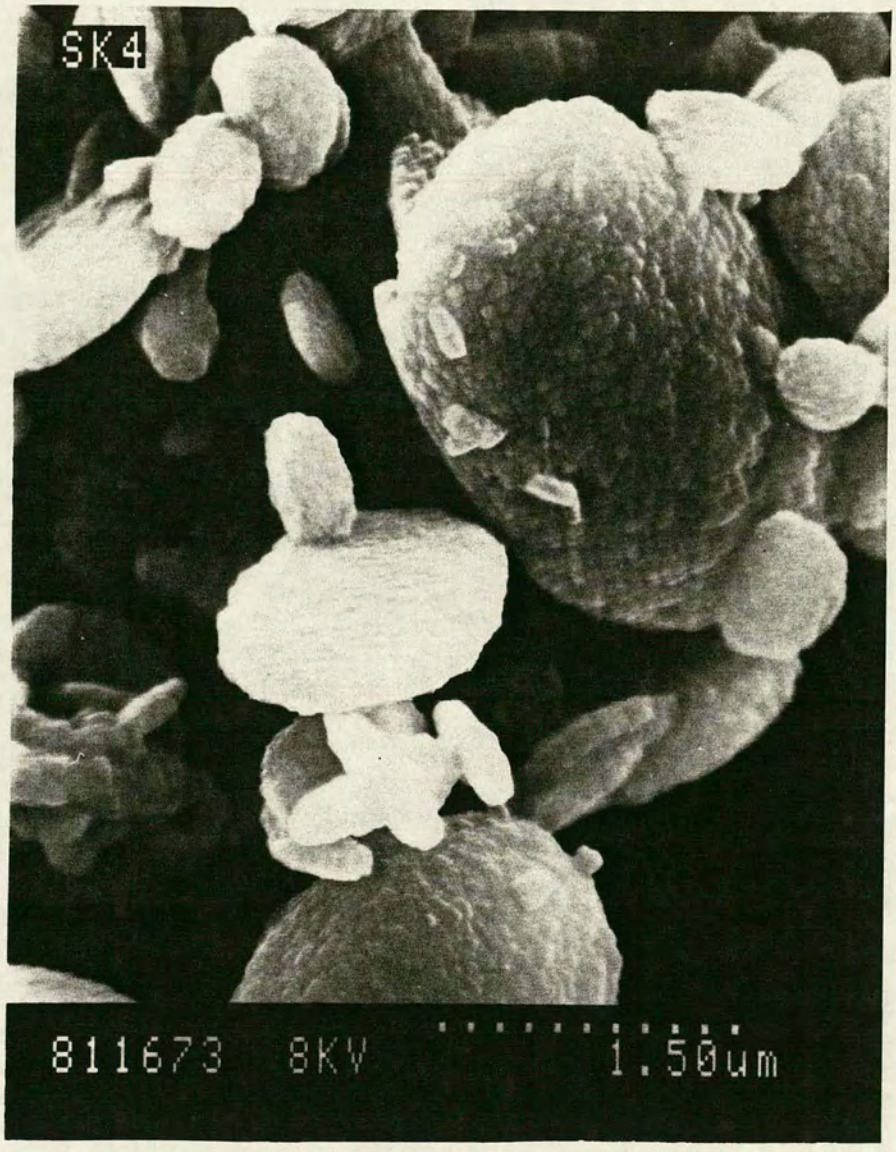


Figure 22

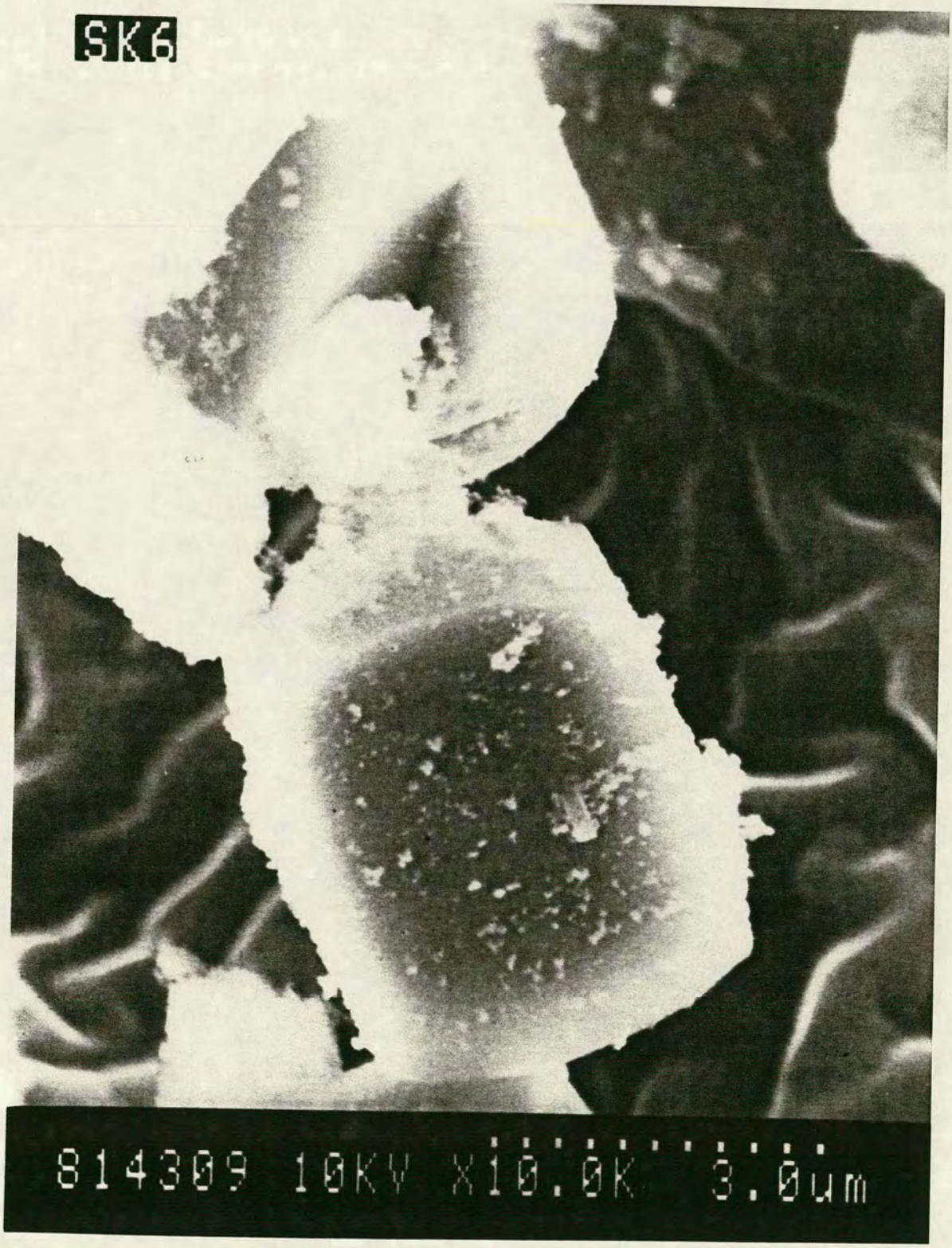


Figure 23

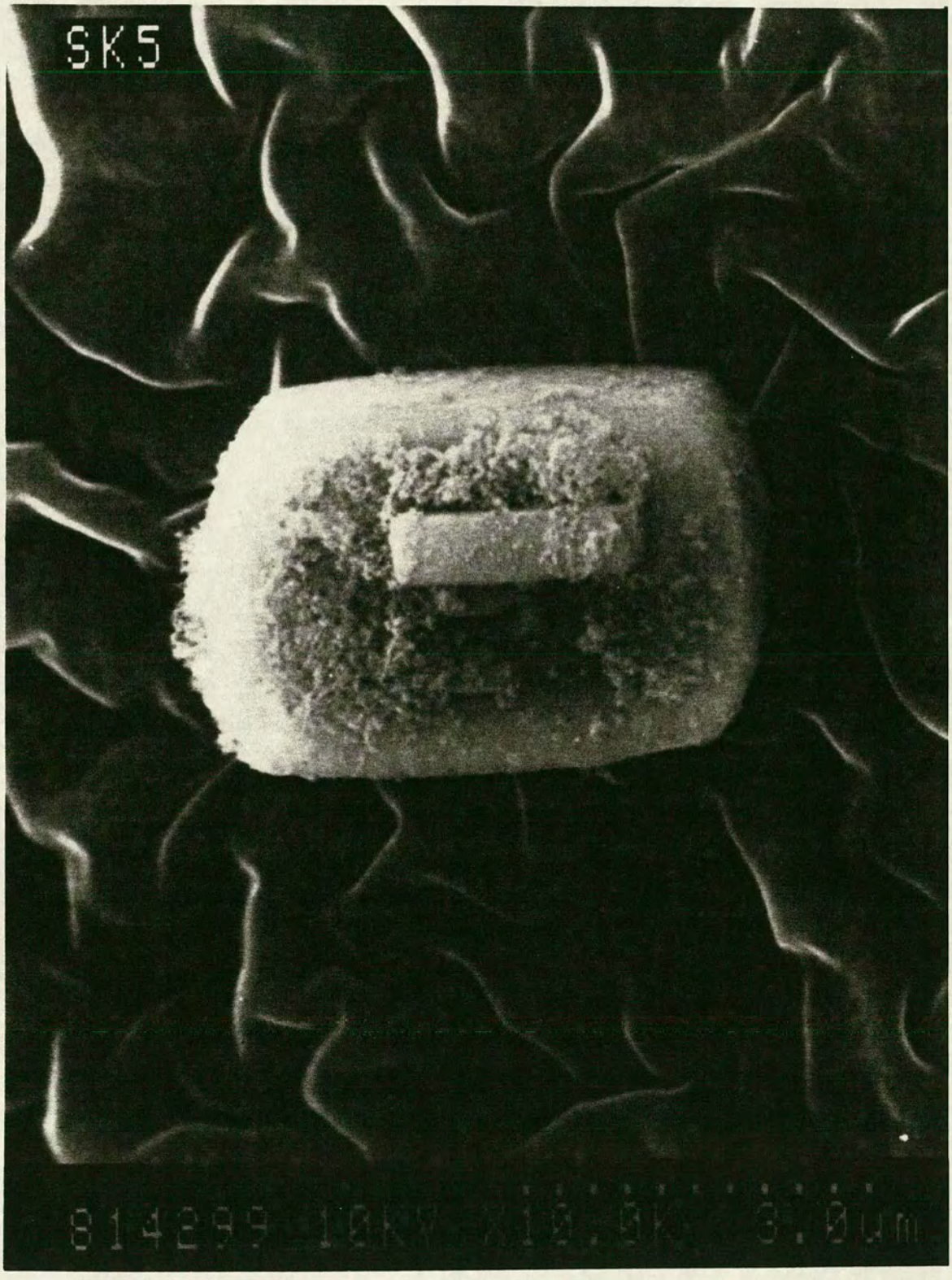


Figure 24

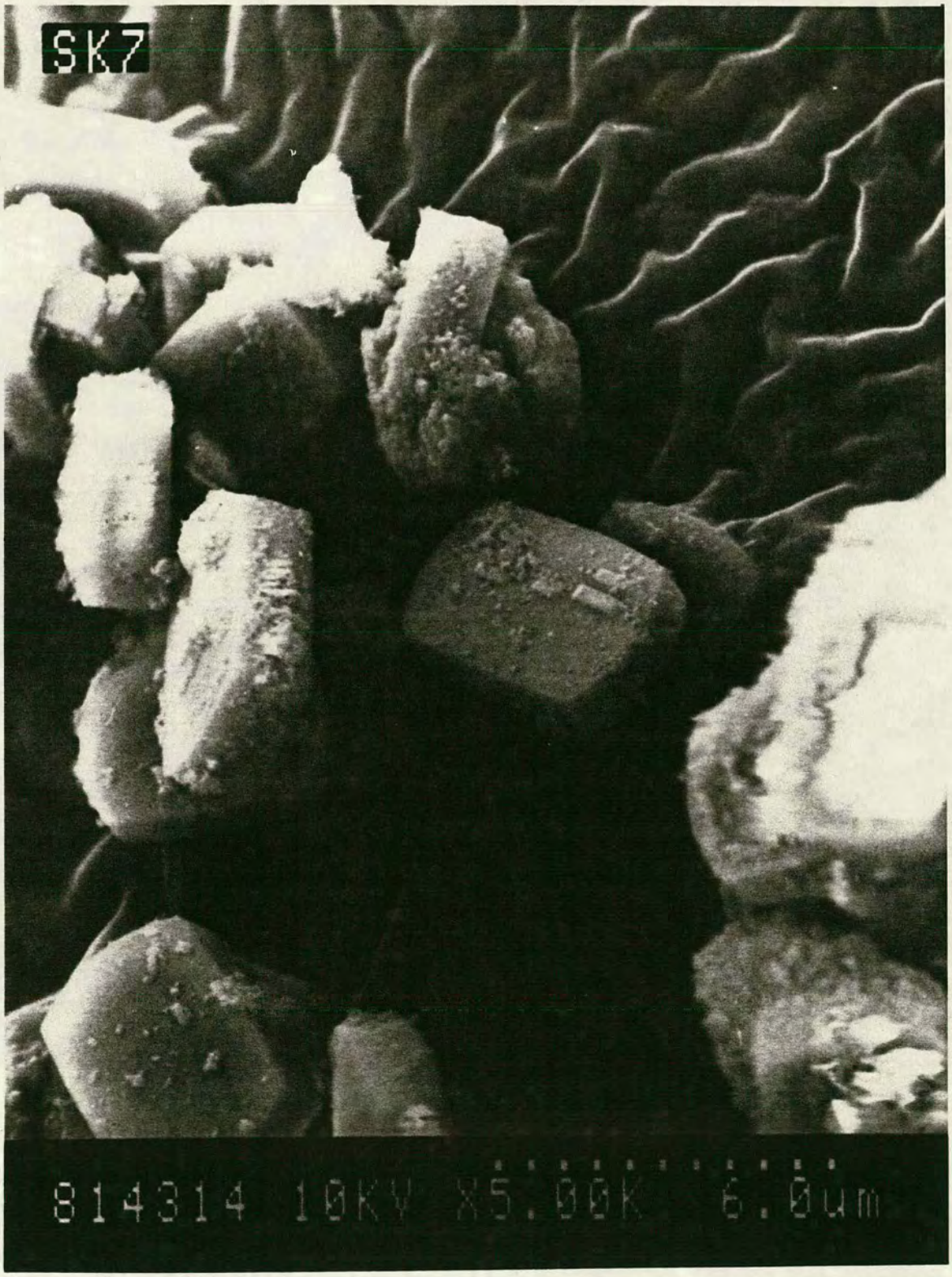


Figure 25

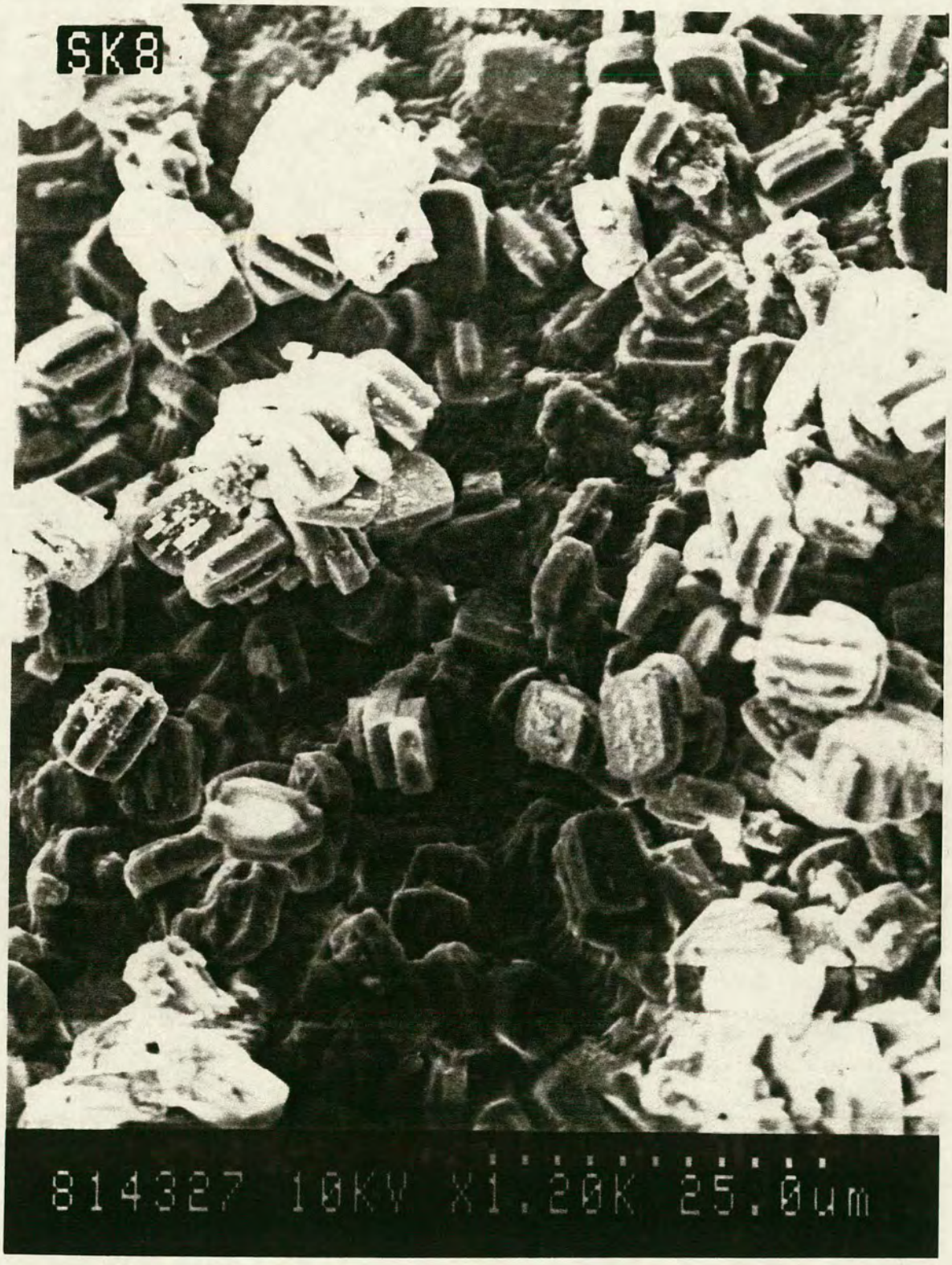


Figure 26

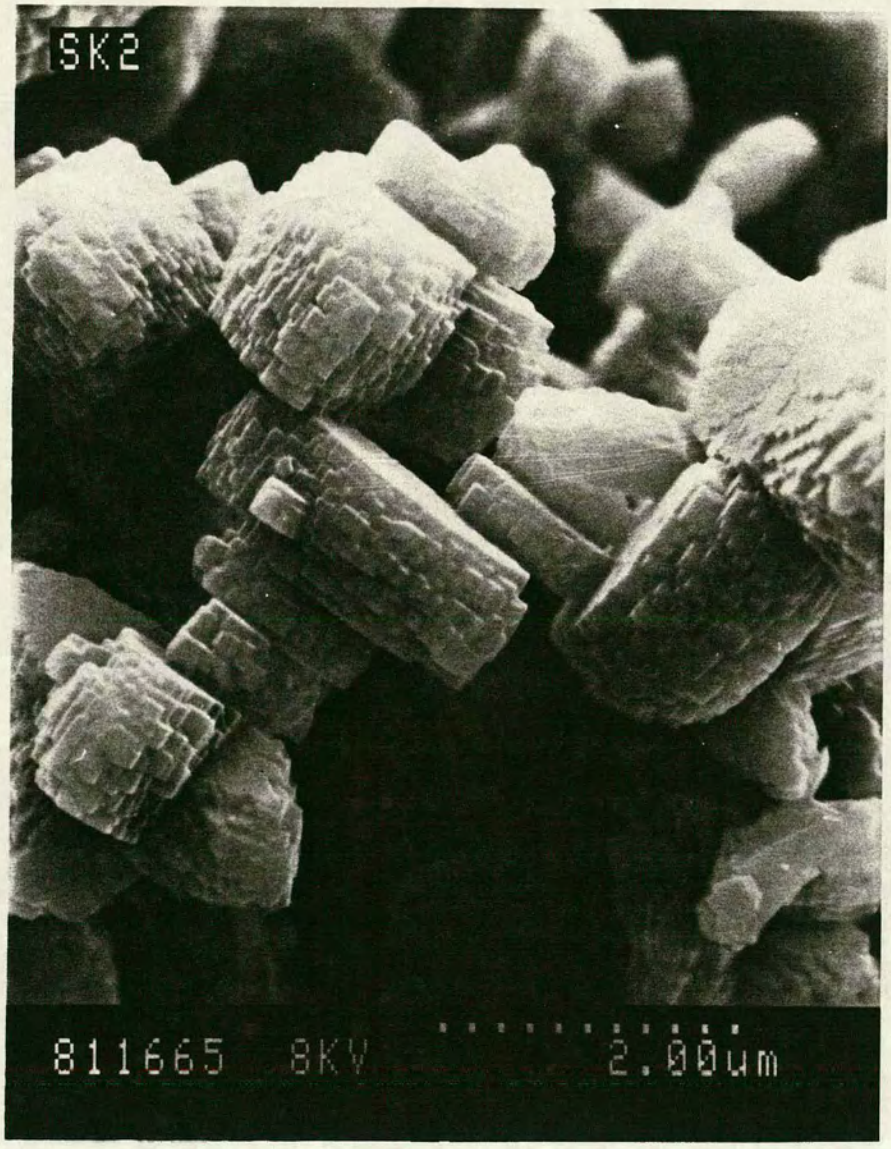


Figure 27

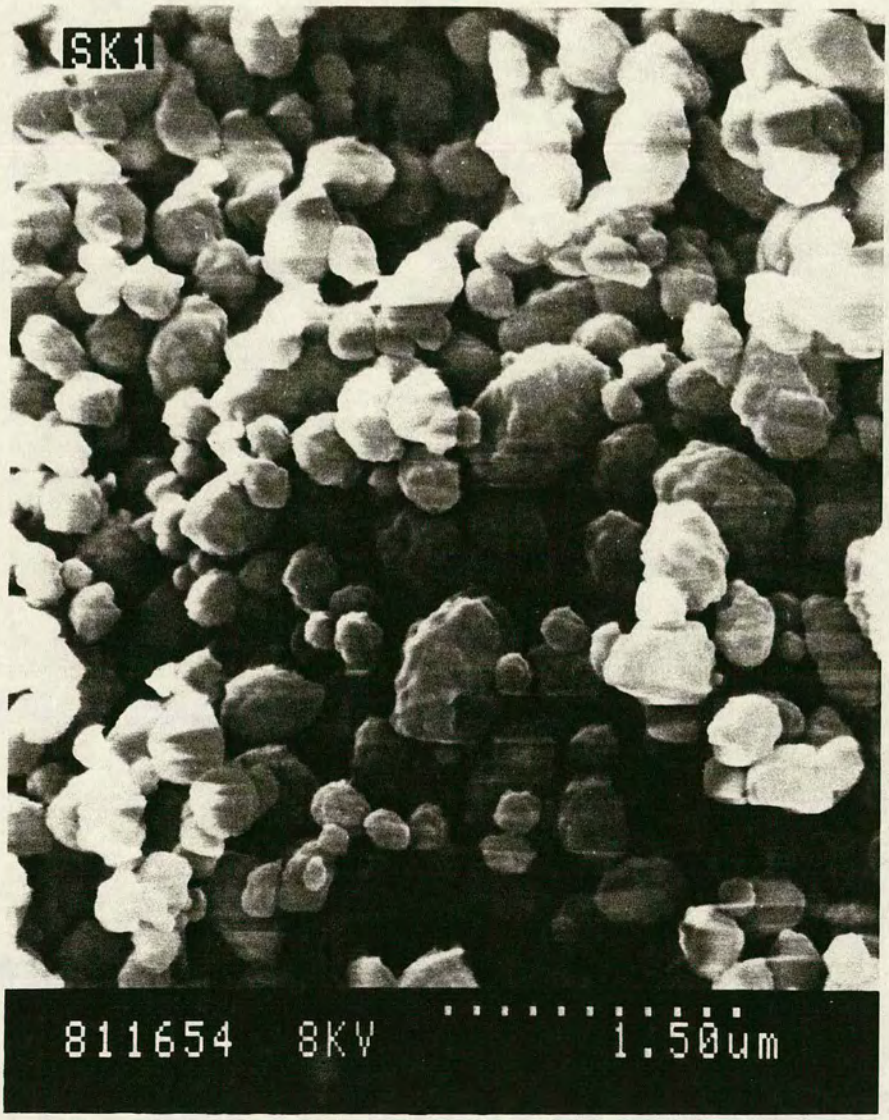


Figure 28

Figure 29

7. EXPERIMENTAL - ORGANIC REACTIONS

7.1 General

7.1.1 Instrumentation

i) Infra red spectroscopy:

I.r. spectra were recorded as nujol mulls or liquid films on a Perkin-Elmer 781 spectrophotometer.

ii) Mass spectroscopy:

Mass spectra and g.c.-m.s. were obtained on an AEI MS902 or a Kratos MS 50TC instrument by Mr A Thomson and Miss E Stevenson.

iii) Melting points were measured in open capillary tubes using a Gallenkamp MFB595 apparatus.

iv) ^{1}H NMR spectra were recorded on three Bru ker instruments: WP80, WP200 and WH360 by Miss H Grant, Mr J Millar and Dr D Reed,

^{13}C NMR spectra were recorded on a Bru ker WP200 spectrometer by Mr J Millar.

Chemical shifts (δ) in parts per million downfield from tetramethylsilane (δ = 0.00).

v) Ultra violet spectroscopy:

U.v. spectra were recorded using a Pye-Unicam SP8-400 spectrophotometer.

vi) Gas chromatography (g.c.):

All g.c. analyses were performed on a Pye Unicam GCD instrument with flame ionisation detector, with peak integration by a Hewlett Packard 3373B integrator. Nitrogen was the carrier gas in all cases.

vi) High performance liquid chromatography (h.p.l.c.):

All h.p.l.c. analyses employed a Cecil CE 212 UV monitor set at 254nm for peak detection, linked to a chart recorder and a Venture Mark II digital integrator.

7.1.2 Equipment

All reactions in the presence of zeolites/Nafion-H in Sections 7.2-7.5 were performed in specially designed glass reaction vessels. These consisted of flat bottomed tubes with side-arms which were sealed with Rotaflow taps. The side-arms were employed for reactions under dry conditions where the zeolite in the reaction vessel was further dried under vacuum to remove residual water. The vessels were fitted with B10 Quickfit condensers and silica-gel drying tubes.

The vessels were heated, with magnetic stirring, in a specially designed, insulated aluminium block which was fitted on a top of the heating block of a Gallenkamp hot-plate stirrer. The temperature of the block was monitored *via* a thermocouple and maintained at constant temperature.

7.2 Claisen rearrangement of allyl phenyl ether

7.2.1 Authentic samples

i) Allyl phenyl ether, 2-allylphenol:

These are commercially available (Aldrich) and were distilled and stored over 4A molecular sieve.

ii) 4-allylphenol:

This material was prepared by the method of Quelet[208] in two stages. Grignard reaction of 1,4-dibromobenzene (23.64g, 0.100mol) in 95ml of sodium-dried ether, with magnesium (2.72g, 0.113 mol) and allylbromide (13.0g, 0.107 mol) gave 7.06g (35.8%) of 1-bromo-4-allylbenzene. After distillation, the pure product was employed in a second Grignard reaction. 1-bromo-4-allylbenzene (3.60g, 0.018 mol) was dissolved in 10ml of sodium-dried ether. Magnesium filings (0.50g, 0.020 mol) were added and the mixture left without stirring for 108h at room temperature, protected from moisture by a silica-gel guard tube. In an ice salt bath dry oxygen was passed through the mixture and the complex was decomposed with crushed ice.

After work-up, 0.570g of crude product was obtained. Kugelrohr distillation gave 0.380g of a yellow liquid which showed two spots by t.l.c. By flash chromatography, eluting with ethyl acetate-hexane (15:85), 4-allylphenol

was isolated as a clear liquid (0.121g, 4.9%). *m/z* 134 (M^+);

νmax 3720 - 3120 cm^{-1} (OH); δ_H/(80MHz, $CDCl_3$) 6.6 - 7.2 (4H,m,ArH), 5.98 (1H, tdd, J 6.5, 9.3, 11.0 Hz, -CH=) 5.06 (2H,m,=CH_2) 3.32(2H,d,J 6.5 Hz,CH_2); δC (50 MHz, $CDCl_3$) 153.4 (C-OH), 137.7 (CH), 132.2 (ArC), 129.6 (2 x ArC) 115.3 (=CH_2), 115.2 (2 x ArC), 39.1 (CH_2).

iii) 2-Methyldihydrobenzofuran:

This compound was prepared by the method of Tarbell.[209] 2-allylphenol (8.5ml, 0.065mol) was refluxed with acetic acid (34ml) and 48% aqueous HBr (17ml) to yield 6.513g of crude product. After distillation, 1.910g (21.8%) of pure 2-methyldihydrobenzofuran was obtained as a clear liquid b.p. 82-85°C/10mm Hg (lit[209] 86.5-87.5/19mm Hg); *m/z* 134 (M^+); δH (80MHz, $CDCl_3$) 6.8 - 7.4 (4H, m, ArH), 4.99 (1H, ddq, C*H*(Me)) 3.28 (1H, dd, *J* 8.7 Hz, $J_{Ha,Hb}$ 15Hz, CH_2 (Ha)), 2.96 (1H, dd, *J* 7.7 Hz, $J_{Ha,Hb}$ 15Hz, CH_2 (Hb)), 1.57 (3H, d, Me); δC (50 MHz, $CDCl_3$) 159.3 (ArC), 127.5 (ArCH), 126.6 (ArC), 124.6, 119.7, 108.9 (ArCH), 78.9 (*C*H(Me)), 36.7 (CH_2), 21.3 (Me).

7.2.2 Catalysts

i) Zeolite synthesis and preparation as Section 6.

ii) Nafion-H - Nafion NR50 ex Aldrich (E I Du Pont), mesh size 10-35.

Note: In Fries chapter, Nafion-H (smaller mesh size (60-80) was employed) but not available when Claisen work performed.

7.2.3 General reaction procedure for stirred reactions

Allyl phenyl ether (APE) and the catalyst were weighed into the reaction vessels in a 5:1 w/w ratio, typically 7.5g APE to 1.5g zeolite, and heated, with stirring at the required temperature for 48h. In those reactions which were monitored with time, samples were removed by pipette through the condenser. Stirring was maintained during sampling to ensure an even distribution of zeolite and product mixture. The weights of each sample and the residue in the pipette were recorded, thus establishing the total weight removed from each reaction mixture. After 48h, the final product was allowed to cool and centrifuged to remove the zeolite. The product mixture was shaken with acetone (30ml), centrifuged and the acetone layer decanted off.

The process was repeated a further three times, the combined acetone layers were dried over magnesium sulphate and the solvent evaporated under vacuum. In each case, the starting weights of APE and catalyst, the total weight of samples removed and the final yields obtained after separation from the zeolite are shown in Table 38. It should be noted that a larger amount of APE was utilised with Nu-10 zeolites to enable the mixtures to be stirred. Nu-10 occupied a considerably larger volume w/w than the other zeolites in this study.

Those samples taken from the reaction mixtures at set times were also worked up to remove zeolite. In those reactions marked in Table 38, the samples were centrifuged as described above. The other samples indicated were dissolved in acetone and expelled by syringe through organic resistant microfilters (0.2μm mesh, Aerodisc CR, obtained from Gelman Sciences). The filters were rinsed with further acetone, the samples dried over magnesium sulphate and the solvent evaporated under vacuum.

7.2.4 Reaction of 2-allylphenol (2-AP) over zeolites

A similar method to that described in section 7.2.3 was employed. The 2-allylphenol and zeolite were heated for 48h at 140°C. These reactions were not monitored with time. The initial weights of zeolite, 2-AP and the product yields are shown in Table 39.

7.2.5 Procedure for sorption reactions

APE was sorbed onto zeolites in a 1:3 w/w ratio by the following general procedure. The APE was dissolved in methylene chloride (10ml per 0.2g) and a known weight of

Table 38 Claisen rearrangement of allyl phenyl ether (APE)

catalyst	T (°C)	wt.catalyst (g)	wt.APE (g)	total sample[a] wt (g)	final[b] yield (g)
Na-Y	140	1.49	7.55	1.10[c]	6.46
Na-A	140	1.49	7.50	1.08[c]	6.53
(Na,H)-Nu-10(WZ 285)	140	1.49	10.01	1.32[d]	8.25
(Na,H)-EU-1	140	1.52	7.51	0.93[d]	6.53
(Cu(II),H)-Y	140	1.50	7.49	0.91[c]	6.36
$AlPO_4$-5	140	1.50	7.50	1.07[c]	6.21
H-Nu-2	140	1.00	5.00	-[e]	4.67
H-ZSM-5(SKH-Z2)	140	1.02	5.00	-[e]	4.98
None	140	-	5.02	-[e]	4.69
H-Nu-2	100	1.51	7.50	1.28[d]	6.23
H-EU-1	100	0.89	4.50	1.16[d]	3.52
H-Nu-10(WX 149 CX)	100	1.51	10.00	1.58[d]	8.37
H-ZSM-5 (SKH-Z2)	100	1.49	7.52	0.87[d]	6.74
H-ZSM-5 (SKH-Z1)	100	1.50	7.51	0.80[d]	6.44
H-ZSM-5 (SKH-Z3)	100	1.50	7.51	1.04[d]	6.46
H-ZSM-5 (SKH-Z4)	100	1.50	7.51	0.82[d]	6.36
(Cu(II),H)-Y	100	1.50	7.51	1.05[d]	6.61
Nafion NR50 (Nafion-H)	100	1.50	7.51	1.01[d]	6.61
None	100	-	5.01	-[e]	4.95

Table 39 Reaction of 2-allylphenol (2-AP)

catalyst	T (°C)	wt.catalyst (g)	wt.APE (g)	total sample wt (g)	final[b] yield (g)
Na,H-EU-1	140	0.75	3.76	-[e]	3.72
None	140	-	3.76	-[e]	3.54

a total weight of all samples removed from reaction mixture, incl. both zeolite & organic
b product yield after removal of zeolite
c zeolite removed from samples by centrifuge
d zeolite removed from samples by microfiltration
e no samples taken

zeolite was stirred into the solution. The solvent was evaporated under vacuum to yield a slightly moist powder. A portion of the powder was weighed into a reaction tube which was sealed and heated at 140°C for 5h. Some material evaporated onto the walls of the tube. The product was removed from the zeolite by continuous extraction in a Soxhlet apparatus with methylene chloride. Table 40 shows the weights of APE and zeolite in the batch, the weight of the portion of sorbed material and the starting weight of APE in this portion.

7.2.6 General analysis procedure

Analysis of the product mixtures of 7.2.4 and 7.2.5 was performed by h.p.l.c. by the internal standard technique and by g.c.

i) h.p.l.c.:

h.p.l.c. analyses were performed using a reverse phase ODS/Hypersil column with methanol/water (70:30) as eluent.

Quantitative analyses were made by the internal standard method. From three calibration mixtures, a correction factor K_X was determined for each component.

$$K_X = \frac{W_X A_{is}}{W_{is} A_X}$$

W_X = weight of the component (g)

W_{is} = weight of internal standard (g)

A_X = area of component peak

A_{is} = area of internal standard peak

Table 40 Rearrangement of APE by sorption technique

zeolite	wt.zeolite (g)	wt.APE (g)	wt.sorbed portion (g)	wt.starting[a] APE (g)	yield (g)
(Na,H)-ZSM-5(Rblb)	0.407	0.141	0.248	0.064	0.0347
Na-Y	0.601	0.205	0.366	0.093	0.0598
Na-A	0.601	0.212	0.388	0.101	0.0892
(Na,H)-Nu-10(AA53)	2.406	0.820	0.385	0.098	0.0742

a weight APE in sorbed portion

Product samples were prepared with a known weight (approx 0.1g) of product and 0.0803g of internal standard from a standard solution in methanol. Each sample was injected until concordant peak area ratios (±3%) were obtained. The weight % of each component in the product samples was calculated as follows:

$$\% X = \frac{K_X W_{is} A_X}{A_{is} W_S} \times 100\%$$

where W_S = weight of product sample (g)

Using the above h.p.l.c. conditions, 4-allylphenol (4-AP) was eluted underneath the 2-AP peak. Therefore, the yield of 4-AP was determined by g.c. The u.v. absorbances of 2-AP and 4-AP were measured at 254nm. The extinction coefficients were calculated to be 40.6 and 42.3 respectively, thus the ratio of 2-AP/4-AP determined by g.c. could be directly transferred to the h.p.l.c. weight % result.

ii) g.c.:

G.c. analyses were performed on a 1m Tenax g.c. column under a temperature programme at 180°C for 10 min, increasing by 8°C/min to 300°C.

The ratio of 2-AP to 4-AP in each sample was determined as follows:

$$\frac{2\text{-AP}}{4\text{-AP}} = \frac{A_{2\text{-AP}}}{A_{4\text{-AP}}} \times \frac{K_{2\text{-AP}}}{K_{4\text{-AP}}}$$

$A_{2\text{-AP}}$ = area of 2-AP peak

A_4-AP = area of 4-AP peak

$\frac{K_{2\text{-AP}}}{K_{4\text{-AP}}}$ = relative correction factors of 2-AP and 4-AP determined from calibration samples.

7.2.7 Calculation of mol % results

By the analytical procedures described above, the weight % of phenol, 2-AP, 4-AP, DBF and APE in each sample and in the final product was determined. An example is illustrated in Table 4 for the rearrangement of APE over H-Nu-2 at 100°C.

Table 41 Rearrangement of APE over H-Nu-2 at 100°C - yields as weight % of recovered product

time (h)	2-AP	4-AP	DBF	ph (wt %)	APE	total
1	26.4	1.7	3.3	5.3	63.4	98.1
4	34.5	2.3	7.8	5.0	50.3	99.9
8	37.0	2.3	8.5	4.8	43.6	96.2
24	34.6	2.2	18.0	5.2	31.0	91.0
48	32.4	2.3	25.8	4.6	22.9	88.0

As the total weight of starting materials (APE and catalyst) was known and the total weight of samples removed from the reaction over mixture was recorded (Table 38) the final weight of the reaction mixture could be calculated, e.g. in the reaction H-Nu-2 at 100°C, the starting materials were 7.50g of APE and 1.51g of zeolite, from which a total weight of 1.28g of samples were removed. Thus the final weight of the reaction mixture was 7.73g. In this, the proportion of organic material would be 7.50/9.01, that is 6.43g. This weight was taken to be the starting weight of allyl phenyl ether (0.0480 moles) from which was isolated the final yield shown (Table 38). It is assumed that when each of the smaller samples was worked up to remove zeolite that the same proportion of product would be recovered. The mole % of each component based on initial APE was calculated:

$$\text{mol \% X} = \frac{\text{wt \% X} \times \text{final yield}}{MW_X \times \text{moles (initial APE)}}$$

eg. after 1h

$$\text{mol \% 2-AP} = \frac{24.4 \times 6.23}{134 \times 0.0480} = \underline{23.6\%}$$

7.2.8 ^{13}C n.m.r. of reaction products

The presence of APE, 2-AP, 4-AP and DBF in the reaction products was confirmed by ^{13}C n.m.r. in selected examples. From the spectra of authentic samples (200MHz, $CDCl_3$) the following characteristic peaks were identified:

APE δ 68.4 (CH_2), 133.2 (CH)

2-AP 34.4 (CH_2), 136.2 (CH)

4-AP 39.1 (CH_2), 137.7 (CH)

DBF 21.3 (Me), 36.7 (CH_2), 78.9 (CH)

Table 42 shows those characteristic peaks which were observed in the ^{13}C n.m.r. spectra of the product mixtures. Thus the presence or absence of the above components in the product mixtures (after 48h) was confirmed.

7.3 Fries rearrangement of phenyl acetate

7.3.1 Authentic Samples

i) Phenyl acetate is commercially available (Aldrich) and was distilled and stored over 4A molecular sieve.

ii) 2-Hydroxyacetophenone (2-HAP) is commercially available (Aldrich) and was distilled and stored over 4A molecular sieve.

iii) 4-Hydroxyacetophenone (4-HAP) is commercially available (Aldrich) and was recrystallised from ethanol.

iv) Phenol is commercially available (Aldrich).

v) 2-Acetoxyacetophenone (2-AAP).

This material was prepared by a modification of a general procedure for the preparation of phenol acetates.[210] 2-

Table 42 ^{13}C n.m.r. analysis of product mixtures (50Mz, $CDCl_3$)

catalyst	T (^oC)	(ppm) 20 - 80						132 - 140		
(Na,H)-Eu-1	140	21.2	34.2	36.6	39.0	68.4	79.2	133.0	136.3	137.6
(Cu(II),H)-Y	140	21.2	34.2	36.6	39.0	68.4	79.2	133.0	136.3	137.6
H-Nu-2	100	21.2	34.2	36.6	39.0	68.4	79.2	133.0	136.3	137.6
H-EU-1	100	21.2	34.2	36.6	-[a]	68.3	79.1	133.1	136.4	-[a]
H-Nu-2	140	21.6	34.6	37.0	39.6	68.8	79.6	133.5	136.7	-[b]
H-ZSM-5 (SKH-Z2)	140	21.6	34.6	37.0	-[a]	68.7	79.4	133.4	136.6	-[a]

a not present
b may be obscured by messy baseline

Hydroxyacetophenone (10.5g, 0.077 mol) was dissolved in 1M NaOH (110ml). Crushed ice (100g) was added to the solution, followed by acetic anhydride (20ml, 21.6g, 0.212 mol) and the mixture shaken vigorously for 1 min. The white solid was removed by filtration and recrystallised from dilute ethanol (yield 93.6%). m.p. 87.8 - 88.9°C (lit.[212] 89°C); ν_{max} (nujol) 1760cm^{-1} (ester C=O) 1688cm^{-1} (ketone C=O); δ_H (80MHz, $CDCl_3$) 7.0 - 7.8 (4H, m, ArH) 2.50 (3H, s, Me) 2.29 (3H, s, Me); δ_C (50MHz,$CDCl_3$) 197.2 (C=O) 169.1 (C=O) 148.9 (ArC) 133.2 (ArCH) 130.6 (ArC) 130.0, 125.8, 123.6 (ArCH) 29.1 (Me) 20.9 (Me); *m/z* 178 (M^+).

vi) 4-Acetoxyacetophenone (4-AAP):

This material was prepared by the above procedure from 4-hydroxyacetophenone. The white solid was recrystallised from dil. ethanol (yield 95.4%), m.p. 50.2 - 52.0°C (lit.[211] 54°C); ν max (nujol) 1756 cm^{-1} (ester C=O) 1677 cm^{-1} (ketone C=O); δ H(80MHz, $CDCl_3$) 7.1 - 8.0 (4H, M, ArH) 2.52 (33H, S, Me) 2.25 (3H, S, Me); δ C(50MHz , $CDCl_3$) 196.5 (C=O) 168.5 (C=O) 154.2, 134.5 (ArC) 129.6, 121.5 (ArCH) 26.2 (Me) 20.8 (Me); *m/z* 178 (M+).

vii) 2-Methylchromone (2-MeCH):

This product was prepared by the method of Wittig <u>et al</u>.[212] Condensation of 2-hydroxyacetophenone (10.51g, 0.077 mol) with ethyl acetate (40ml, 36.1g, 0.410 mol) in the presence of sodium (4g, 0.174 mol) gave an

intermediate β-diketone which was directly cyclised to 2-methylchromone with conc. sulphuric acid (50ml) (yield 30.1%). The product was recrystallised from pet. ether (60-80) as white needles. m.p. 70.9 - 72.0°C (lit[211] 72-73°C); ν_{max} (nujol) 1669cm^{-1} (C=O); δ_H (200MHz,$CDCl_3$) 8.1 - 7.2 (4H, m, ArH) 6.07 (1H, q, CH) 2.28 (3H, d, Me); δ_C (50MHz, $CDCl_3$) 177.9 (C=O) 166.0 (CMe) 156.2 (ArC) 133.2, 125.3, 124.6 (ArCH) 123.3 (ArC) 117.6 (ArCH) 110.3 (CH) 20.3 (Me); *m/z* (160) M^+.

viii) 4-Methylcoumarin (4-MeC):

This product was prepared by the method of Woodruff[213] via the condensation of phenol (22.0g, 0.234 mol) and ethylacetoacetate (31ml, 31.4g, 0.234 mol) in the presence of aluminium chloride (62.4g, 0.468 mol). The product was recrystallised as white needles from pet. ether (60-80), (yield 10%); m.p. 75.8 - 77.9°C (lit[214] 82°C); ν max (nujol) 1730cm^{-1} (C=O); δH (200 MHz, $CDCl_3$) 7.6 - 7.1 (4H, m, ArH) 6.20 (1H, q, CH) 2.37 (3H, d, Me); δC(50MHz, $CDCl_3$) 160.5 (C=O) 153.2 (ArC) 152.2 (CMe) 131.5, 124.3, 123.9 (ArCH) 119.7 (ArC) 116.7 (ArCH) 114.8 (CH) 18.6 (Me); *m/z* 160 (M^+).

7.3.2 Catalysts

i) Zeolite synthesis and preparation as section 6.

ii) Nafion-H ex. Aldrich (E I Du Pont) 60 - 80 mesh size.

7.3.3 General procedure for rearrangement of phenyl acetate

Phenyl acetate and the catalyst were employed in 5:1 w/w ratio, typically 7.5g phenyl acetate to 1.5g catalyst. The reaction vessels were fitted with a condenser and silica gel drying tube and heated, with stirring at the required temperature. An exception was the reaction over H-Nu-10 which could not be stirred as all the liquid was sorbed by the zeolite. In those reactions which were monitored with time, samples were taken by pipette through the condenser. Stirring was maintained to ensure even distribution of the zeolite and organic in the samples. The weight of each sample and of the residue in the pipette was recorded, so the total weight removed was known. After the required time, the product mixture was allowed to cool and centrifuged to remove the catalyst. The product mixture was shaken with acetone (30ml), centrifuged and the acetone layer decanted off. The process was repeated a further three times, the combined acetone layers were dried over magnesium sulphate, filtered and the solvent evaporated under vacuum. For each reaction, the starting weights of phenyl acetate and catalyst, the total weight of samples removed and the final yield after separation from the catalyst have been recorded (Table 43).

Table 43 Reaction conditions and isolated yields (rearrangement of phenyl acetate)

catalyst	comments	T (°C)	time (h)	wt.catalyst (g)	wt.phenyl acetate (g)	total samples removed (g)	isolated yield (g)
H-Nu-2	-	170	52	1.51	7.51	1.87	4.86
H-ZSM-5(Rblb)	-	170	52	1.51	7.52	2.24	4.81
H-EU-1	-	170	52	1.51	7.51	2.95	3.98
H-Nu-10 (WX 149 CX)	not stirred	210	54	1.00	5.00	0.04	4.14
Na-Y	-	170	52	1.02	7.52	1.51	5.57
H-Nu-2	-	210	52	1.01	5.01	2.06	2.41
H-ZSM-5(Rblb)	-	210	52	1.02	5.00	2.10	2.95
H-Nu-2	regenerated	210	52	0.61	3.01	1.39	1.54
Nafion-H	-	170	52	1.54	7.73	2.39	4.29
(Cu(II),H)-Y	-	210	52	1.50	7.51	2.01	5.23
H-Nu-2	pre-dried	170	52	1.44	7.35	2.39	4.88
None	-	210	52	-	1.03	-	0.95

For g.c. analysis, samples taken from the reaction mixture with time were also worked up to remove zeolite. Each sample was centrifuged with acetone by the procedure described above.

7.3.4 Rearrangement of phenyl acetate over dried H-Nu-2

H-Nu-2 was dried overnight (17h) in a furnace at 400°C, cooled in a vacuum desiccator over phosphorus pentoxide and transferred to the reaction vessel in a glove bag under dry nitrogen. The sealed apparatus was further evaluated at 170°C for 1h (0.2mmHg) before reaction. The vacuum was released under a dry nitrogen blanket and phenyl acetate was added by pipette. The rearrangement was performed at 170°C under a nitrogen blanket with continuous stirring. Samples were taken by pipette through the condenser. After 52h, the product mixture and samples were treated as in section 7.3.3 and analysed by g.c. The total weight of samples removed and the final yield were recorded (Table 43).

7.3.5 Attempted reverse rearrangement of 2- and 4-hydroxyacetophenone

A similar procedure to that described in section 7.3.3 was employed. The neat phenols were stirred with H-Nu-2 in a 2:1 w/w ratio at 210°C for 24h. 4-hydroxyacetophenone rapidly melted under these conditions. The dark, viscous product mixtures were separated from the zeolite by centrifuge (with 5 x 30ml) acetone), dried over magnesium

sulphate and the solvent evaporated under vacuum. The product composition was determined by g.c.

7.3.6 Attempted cyclisation of 2-acetoxyacetophenone to 2-methylchromone and 4-methylcoumarin

Cyclisation was attempted by two methods. Initially, following the general procedure described in section 7.3.3, 2-acetoxyacetophenone (2-AAP, 1.50g, 0.008 mol) was stirred with 1.01g H-Nu-2 at 210°C for 52h. In an attempt to ensure sorption of 2-AAP by the zeolite, the reaction was repeated. 2-AAP (0.75g, 0.004 mol) was dissolved in 10ml of methylene chloride. H-Nu-2 (1.50g) was stirred into the solution and the solvent slowly removed under vacuum. The dry powder was heated at 210°C for 52h. In both experiments the products were extracted by centrifuge (4 x 30ml acetone) and analysed by g.c. Only traces (<0.1%) of 2-methylchromone and 4-methylcoumarin were detected by g.c. In each case a brown liquid was isolated and g.c. indicated the major product to be 2-hydroxyacetophenone and the absence of 2-AAP.

7.3.7 Attempted condensation of 2-hydroxyacetophenone with acetic acid

2-hydroxyacetophenone (0.57g, 0.004 mol) and acetic acid (0.50g, 0.008 mol) were stirred with H-Nu-2 (1.00g) at 210°C for 52h. The product was separated from the zeolite by centrifuge (4 x 30ml acetone), dried over magnesium

sulphate and the solvent removed under vacuum. By g.c., 2-methylchromone and 4-methylcoumarin were not detected.

7.3.8 General analysis procedure

Analysis of the product mixtures of 7.3.3, 7.3.4, 7.3.5, 7.3.6 was performed by g.c. by the internal standard technique and by h.p.l.c.

i) g.c.:

G.c. analyses were performed on a 1m Tenax GC column under a temperature programme at 180°C increasing by 4°C/min to 300°C.

Quantitative analyses were made by the internal standard method as detailed in sections 7.2.6 and 7.2.7.

During the course of this study, it was discovered that under the g.c. conditions employed, 4-acetoxyacetophenone (4-AAP) was eluted directly underneath the peak attributed to 4-HAP. Thus the 4-AAP content was determined by reverse phase h.p.l.c. from the ratio of 4-HAP to 4-AAP. By g.c., the correction factor K_x for 4-HAP and 4-AAP was the same so the ratio calculated by h.p.l.c. could be applied directly to the g.c. results.

ii) h.p.l.c.:

h.p.l.c. analyses were performed using a reverse phase ODS/Hypersil column with methanol/water (70:30) as eluent.

$$\text{Ratio:} \quad \frac{\text{4-HAP}}{\text{4-AAP}} = \frac{A_4\text{-HAP}}{A_4\text{-AAP}} \times \frac{K_4\text{-HAP}}{K_4\text{-AAP}}$$

A_4-HAP = area of 4-HAP peak
A_4-AAP = area of 4-AAP peak

7.4 Fries rearrangement of phenyl benzoate

7.4.1 Authentic samples

Phenyl benzoate, 2-hydroxybenzophenone and 4-hydroxybenzophenone were commercially available (Aldrich).

7.4.2 General procedure for rearrangement of phenyl benzoate (stirred reactions)

An identical procedure to that described in Section 7.3.3 was employed with phenyl benzoate in the melt. For each reaction, the total weight of samples removed and the final yield after separation from the catalyst have been recorded (Table 44).

7.4.3 General procedure for the rearrangement of phenyl benzoate (sorbed reactions)

Phenyl benzoate was sorbed onto zeolites in a 1:1 w/w ratio by the following procedure: The phenyl benzoate (1g) was dissolved in methylene chloride (20ml) and the zeolite (1g) was stirred into the solution. The solvent was evaporated under vacuum to yield a dry powder. A portion of the powder was weighed into a reaction tube and heated at 210°C for 24h.

Table 44 Fries rearrangement of phenyl benzoate (stirred reactions, 72h)

catalyst	T (°C)	wt.catalyst (g)	wt.phenyl benzoate (g)	total sample[a] wt. (g)	final yield[b] (g)
H-Nu-2	210	1.51	7.54	3.45	4.46
H-ZSM-5(SKH-Z2)	210	1.51	7.52	2.73	5.02
H-EU-1	210	1.50	7.56	2.60	4.91
Na-Y	210	1.50	7.50	-[c]	7.28
Nafion-H(NR50)	210	1.53	7.57	1.41	5.53
None	210	-	2.49	2.60	4.91
H-Nu-2	140	1.51	7.50	1.93	5.81
Nafion-H(NR50)	140	1.50	7.53	1.42	5.92

a total weight of all samples removed from reaction mixture, including both zeolite and organic
b product yield after removal of zeolite
c no samples taken

Table 45 Fries rearrangement of phenyl benzoate (sorbed reaction, 24h)

catalyst	T (°C)	wt.catalyst (g)	wt.phenyl benzoate (g)	wt.sorbed[a] portion	isolated[b] yield (g)
H-Nu-2	210	1.00	1.00	1.87	0.74
H-Nu-2 (pre-dried)	210	1.00	1.00	1.84	0.792
H-ZSM-5	210	1.02	1.00	1.92	0.790
H-EU-1	210	1.01	1.00	1.91	0.893

The product was removed from the zeolite by centrifuge with 4 x 30ml acetone, as described in Section 7.3.3. For each reaction, the starting weights of phenyl benzoate and catalyst, the weight of phenyl benzoate/zeolite powder heated and the final yield after separation from the zeolite have been recorded (Table 45).

7.4.4 General analysis procedure

Analysis of the product mixtures of Section 7.4.2 and 7.4.3 was performed by g.c. by the internal standard technique on a Tenax g.c. column under a temperature programme at 250°C, increasing by 8°C/min to 300°C.

7.5 Aldol condensation over zeolites

7.5.1 Self-Condensation of acetophenone

7.5.1.1 Authentic samples

i) Acetophenone was commercially available and stored over 4A molecular sieve.

ii) ß-methylchalcone.

This material was prepared by the method of Wayne and Adkins[144] via the self-condensation of acetophenone catalysed by aluminium tert-butoxide. The product was obtained after distillation as a yellow liquid (yield 58%), b.p. 136-138°C/0.15mmHg (lit[143] 150-155°C/1mmHg).

^1H n.m.r. and g.c. analysis indicated that the product was contaminated with residual acetophenone (ca. 10%). A Nuclear Overhauser Enhancement (NOE) difference experiment (as discussed in Section 4.2) confirmed that *trans*- -methylchalcone was the major product.

δ_H (200 MH_2, $CDCl_3$) *trans*-isomer:- 8.02 (2H,m,ArH) 7.6 - 7.3 (8H, m, Ar) 7.12 (1H, q, CH) 2.62 (3H, d, Me). *Cis*-isomer:- 6.70 (q, CH) 2.32 (d, Me). Most of the *cis*-isomer aromatic signals were obscured underneath the *trans*-isomer peaks.

Integration of the ß-methyl signals at δ 2.62 andδ2.32 respectively gave a *trans/cis* isomer ratio of 96:4 in the crude product. The product was purified by flash chromatography on silica, eluting with ethyl acetate (40-60) pet. ether (10:90). The *trans/cis* isomer ratio of resulting pure ß-methylchalcone was 91:9 (yellow liquid).

ν_{max}. 1656 cm^{-1} (C=O); *m/z* 222 (*M*+).

7.5.1.2 General procedure for the self-condensation of acetophenone in the presence of H-Nu-2

Acetophenone was stirred with H-Nu-2 under the conditions shown in Table 46. In those reactions marked, the condenser contained pre-dried 4A molecular sieve to absorb water produced during the condensation reaction. When cool, the reaction mixtures were shaken with acetone (30ml) and centrifuged to remove the zeolite. The acetone

layer was decanted off, the zeolite shaken with a further 30ml of acetone and the process repeated twice. The combined acetone layers were dried over magnesium sulphate and evaporated under vacuum to afford the zeolite-free product mixture.

In reactions 1-4 and reaction 6 (Table 46) the product mixtures were analysed by g.c. (Table 46) to determine the yields of ß-methylchalcone and unchanged acetophenone. The *trans/cis* isomer ratios of β-methylchalcone in all the product mixtures were determined by ^1H n.m.r. (200 MHz, $CDCl_3$) integration of the ß -methyl doublets (as Section 7.5.1.1). In reactions 1-5, mass spectrometry confirmed the presence of ß-methylchalcone in the product mixtures by a peak at *m/z* 222. No peak at *m/z* 306 corresponding to 1,3,5-triphenylbenzene was observed in any of the reaction mixtures.

In reaction 5, ß -methylchalcone was isolated from the product mixture by flash chromatography. Elution with ethyl acetate - (40-60) pet ether (2:98) gave a yellow liquid in 13% yield from initial acetophenone. Acetophenone was recovered in 56% yield. ^1H n.m.r. integration of the ß -methyl doublets gave a *trans/cis* ratio of 90:10, exactly the same as that determined on the product mixture before isolation of ß-methylchalcone.

δ_H (200MHz, $CDCl_3$) as Section 7.5.1.1; ν_{max} 1657cm^{-1} (C=O); *m/z* 222 (M^+).

Table 46 Self-condensation of acetophenone over H-Nu-2

reaction[a]	T (°C)	time (h)	wt. H-Nu-2 (g)	wt. aceto[b]. (g)	isolated[c] yield (g)
1	120	18.5	1.02	4.02	3.76
2	170	24	1.00	3.00	2.51
3	120	89	1.00	2.07	1.84
4	120	72	1.01	4.00	3.81
5	120	48	1.00	4.00	3.71
6	120	48	-	4.00	3.74

a ref. Table 34
b acetophenone
c isolated product analysed by g.c. (Tenax GC column, 250°C increasing by 8°C/min to 300°C) and/or ^{1}H n.m.r.

7.5.2 Condensation of acetophenone with benzaldehyde

7.5.2.1 Authentic samples

i) Benzaldehyde was commercially available (Aldrich) and stored over 4A molecular sieve.

ii) Chalcone (1,3-diphenyl-2-propen-1-one) was commercially available (Aldrich).

7.5.2.2 Condensation of acetophenone and benzaldehyde in the presence of H-Nu-2

Acetophenone (2.00g, 0.0167 mol) and benzaldehyde (1.77g, 0.0167 mol) were stirred with H-Nu-2 zeolite (1.00g) at 120^{o}C for 48h. Molecular sieve (4A) was placed in the condenser to absorb water produced during the reaction. The product mixture was allowed to cool, shaken with acetone (30ml) andd centrifuged to remove the zeolite. The acetone layer was decanted off, the zeolite shaken with a further 30ml of acetone and the process repeated twice. The combined acetone layers were dried over magnesium sulphate and evaporated under vacuum to yield 3.12g of an orange oil.

The oil was distilled (Kugelrohr) to remove unreacted starting materials to leave an orange, oily solid. By flash chromatography on silica, eluting with methylene chloride - pet. ether (30:70) chalcone was isolated in 75% yield. It was recrystallised from ethanol as yellow

needles. m.p. 54.1 - 55.4°C, mixed m.p. 54.4 - 55.6°C (lit[215] 55-57°C); *m/z* 208 (M^+); i.r. spectrum identical to that of authentic chalcone, νmax. (nujol) 1670cm^{-1} (C=O).

7.5.2.3 Control reaction of acetophenone and benzaldehyde (no catalyst)

By exactly the same procedure as section 7.5.2.2 in the absence of catalyst, acetophenone and benzaldehyde gave a 15% yield of chalcone. m.p. 51.0 - 52.2°C, mixed m.p. 52.0 - 53.5°C, *m/z* 208 (M^+); i.r. spectrum identical to that of authentic chalcone, νmax (nujol) 1669 cm^{-1} (C=O).

7.6 Anthraquinone Synthesis

7.6.1 Authentic Samples

2-Benzoylbenzoic acid (2-BBA) and anthraquinone (AQ) are commercially available (Aldrich).

7.6.2 General procedure for sorption of 2-benzoylbenzoic acid (2-BBA) onto zeolites

Batches of 2-BBA sorbed onto zeolites were prepared in a 2:3 w/w ratio of 2-BBA to zeolite. The 2-BBA was dissolved in methylene chloride (10ml per 0.2g zeolite) and the zeolite was stirred into the solution. The solvent was slowly removed under vacuum to leave dry powder. The batch was divided into portions to ensure consistent starting material and the solid was weighed into reaction tubes and heated at the required temperature. The tubes were left open for 1 minute to

prevent a build-up of pressure and then sealed. It was assumed that the 2-BBA and zeolite were evenly distributed throughout, so that the starting weight of 2-BBA in each portion could be calculated.

7.6.3 Procedure for monitoring reactions by i.r. spectroscopy

The tubes were successively removed from the heating block after the required time and allowed to cool. The contents of each tube, including any material which had sublimed onto the walls, were ground in a mortar and pestle. I.r. samples were run as a nujol mull maintaining approximately the same sample size and consistency.

7.6.4 Preparation of standard samples

Standard samples to estimate the extent of conversion of 2-BBA to AQ by i.r. were prepared by the general procedure described in Section 7.6.3, with the compositions shown in Table 47. The weights of 2-BBA and AQ shown were dissolved in 50ml methylene chloride. The low solubility of anthraquinone required the use of a large liquid/solid ratio. The i.r. spectra were recorded as nujol mulls.

Table 47 Standard i.r. samples

2-BBA:AQ (molar ratio)	wt.2-BBA (g)	wt.AQ (g)	wt.H-Nu-2 (g)
95:5	0.1900	0.0102	0.2981
90:10	0.1803	0.0184	0.3031
70:30	0.1430	0.0545	0.3021
50:50	0.1011	0.0923	0.2995
30:70	0.0604	0.1350	0.3012
10:90	0.0222	0.1662	0.3021
5:95	0.0102	0.1752	0.3010

7.6.5 Cyclisation of 2-BBA over H-Nu-2 monitored by i.r. spectroscopy

Reactions at 170°C and 200°C were performed by the general procedure described in Sections 7.6.2 and 7.6.3. Thus for reaction at 170°C the following procedure was employed: 2-BBA (0.799g, 0.0035mol) was dissolved in 40ml of methylene chloride and H-Nu-2 (1.202g) was stirred into the solution. The solvent was removed under vacuum. 6 x 0.2g samples of this batch were weighed into reaction tubes and heated for the required time. The products were allowed to cool and their i.r. spectra and that of unheated starting material recorded as in Section 7.6.3.

7.6.6 Cyclisation of 2-BBA over dry H-Nu-2 monitored by i.r. spectroscopy

H-Nu-2 (0.602g) was dried at 400°C for 24h and cooled in a vacuum dessicator over phosphorous pentoxide. In a glove bag under dry nitrogen, the dry zeolite was transferred into a solution of vacuum dried 2-BBA (0.400g, 0.0018 mol)

in dry methylene chloride (20ml) distilled from and stored over calcium chloride. The flask was sealed under nitrogen by an adaptor with a closed tap, fitted onto a rotary evaporator and the flask opened under vacuum (5mm Hg). The solvent was removed and the tap re-sealed. Portions were weighed out under dry nitrogen and heated at 200°C. I.r. spectra were run as described in Section 7.6.3.

7.6.7 Cyclisation of 2-BBA over H-Nu-2 and removal of products by extraction

A batch of 2-BBA (1.024g, 0.0045mol) absorbed onto H-Nu-2 (1.500g) was prepared as in Section 7.6.2. A 1.061g portion was heated at 200°C for 2h, and the tube contents continuously extracted with methylene chloride in a Soxhlet apparatus for 24h. Removal of the solvent under vacuum yielded a fluffy yellow solid which was dried in a vacuum dessicator. It was assumed that 2-BBA was evenly distributed throughout the starting sample so the initial weight of 2-BBA could be calculated. Yield 0.369g, 93%; m.p. 271°C, mixed m.p. 271°C (m.p. authentic AQ 283.5 - 285°C). This crude AQ was purified by sublimation to yield yellow needles. Yield 0.305g, 77%; m.p. 280.0 - 281.5, mixed m.p. 281.5 - 282.5°C; $m/_z$ 208 (M^+); i.r. (nujol mull) identical to that of authentic AQ; ^{13}C (50MHz, $CDCl_3$) peaks correspond to those reported in literature.[216]

7.6.8 Cyclisation of 2-BBA over H-Nu-2 at 270° and removal of product by sublimation

A sample of 2-BBA (0.985g, 0.0044mol) sorbed onto H-Nu-2 (from the same batch as Section 7.6.7) was heated at 270°C and sublimed product collected on a cold finger. After 10h, the sublimation appeared to be complete and 0.290g (79%) of yellow needles of anthraquinone were obtained. m.p. 281.0 - 282.5°C, mixed m.p. 281.5 - 283.5°C; $m/_z$ 208 (M^+); i.r. (nujol mull) identical to that of authentic AQ; ^{13}C n.m.r. (50MHz, $CDCl_3$) peaks correspond to those reported in literature.[216]

7.6.9 Cyclisation of 2-BBA over H-ZSM-5 (H-Rblb), H-Nu-10 and H-Mordenite monitored by i.r.

These reactions were performed by the general procedure described in Sections 7.6.2 and 7.6.3. In each case, the final sample in the series was extracted after heating to confirm the results from i.r. analysis. Thus H-ZSM-5, H-Nu-10 and H-Mordenite were extracted after 65, 20 and 20h respectively. In each case, the mass spectrum of the product indicated the presence of unreacted 2-BBA starting material by a peak at $m/_2$ 226.

7.6.10 Attempted cyclisation of 2-BBA in the absence of zeolite

A sample of 2-BBA (0.501g, 0.0022) was heated at 200°C for 20h. The product was extracted from the reaction vessel with methylene chloride and the solvent removed under vacuum. Yield = 0.495g (99% recovery) of unchanged 2-BBA.

m.p. 124-126°C (initial 2-BBA m.p. 127 - 129°C); i.r. (nujol mull) identical to that of authentic 2-BBA; $m/_z$ 226 (M^+).

7.6.11 Attempted conversion of phthalic anhydride and benzene to AQ over H-Nu-2 (sorption technique)

Phthalic anhydride (0.305g, 0.0021 mol) was dissolved in 25ml of acetone and H-Nu-2 (0.456g) was stirred into the solution. The acetone was removed under vacuum and the powder refluxed in benzene (15ml) for 5h. The benzene was removed under vacuum and the residual solid was continuously extracted with methylene chloride in a Soxhlet apparatus for 65h. A white solid was obtained, identified as unchanged phthalic anhydride. Recovery 0.300g (98%). m.p. 127 - 135, m.p. of initial phthalic anhydride 132 - 134°C; i.r. (nujol mull) identical to that of authentic phthalic anhydride; $m/_z$ 148 (M^+).

7.6.12 Attempted conversion of phthalic anhydride and benzene to AQ over H-Nu-2 (solution)

H-Nu-2 (0.500g) was added to a solution of phthalic anhydride (0.255g, 0.0017 mol) in benzene (5ml). The mixture was refluxed for 8.5h, then the benzene removed under vacuum and the residue was continuously extracted with methylene chloride for 17h. Removal of the solvent

under vacuum yielded 0.196g of a white solid which appeared to consist of a mixture of phthalic anhydride and phthalic acid. m.p. 182 - 185°C (m.p. authentic phthalic anhydride 132 - 134°C, (authentic phthalic acid 210°C). $m/_z$ 166, 148.

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PARA-SELECTIVE FRIES REARRANGEMENT OF PHENYL ACETATE IN THE PRESENCE OF ZEOLITE MOLECULAR SIEVES

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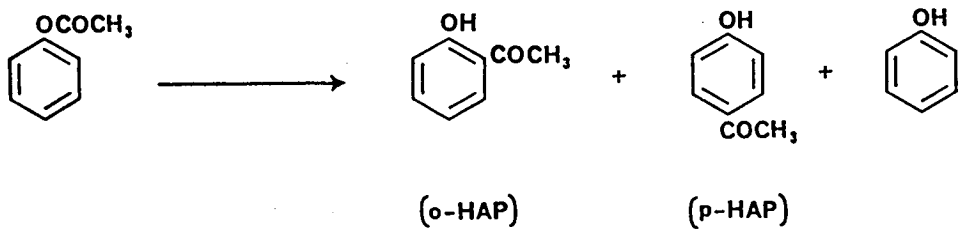
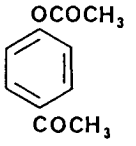
Summary: The Fries rearrangement of phenyl acetate is catalysed by acidic zeolites such as H-Nu-2 and H-ZSM-5, with selectivities of 2-6:1 in favour of para-substituted products.

The Fries rearrangement of phenyl esters affords a mixture of *o*- and *p*-hydroxyphenylketones, together with phenol as a hydrolysis product (Scheme). Extensive research over many years has established that the reaction can be catalysed by a variety of Lewis and Bronsted acids[1,2], with aluminium trichloride being the most widely used. An equimolar amount of $AlCl_3$ is generally required and it is consumed during work up. It is also known that the gas phase reaction can be catalysed by acidic zeolites at high temperatures(*ca* 400 °C)[3,4]. We now report that the liquid phase Fries rearrangement of phenyl acetate is catalysed by acidic high silica zeolites[5] (H-Nu-2[6], unknown structure; H-ZSM-5[7], *MFI* structure) which can be recovered, regenerated and reused, and furthermore that the process shows significant *para*-selectivity.

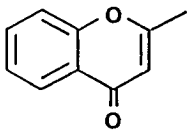


Scheme

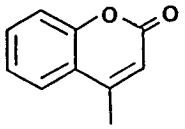
In a typical experiment phenyl acetate (7.5g) and the zeolite (1.5g) were heated together with stirring in the absence of solvent and the progress of the reaction monitored by g.c. and/or h.p.l.c. The results are presented in the Table. With H-Nu-2 after 24h at 170 °C the reaction mixture contained *p*-hydroxyacetophenone(*p*-HAP)(14%), *p*-acetoxyacetophenone (*p*-AAP)(5%), and *o*-hydroxyacetophenone (*o*-HAP)(4%), together with unreacted phenyl acetate (30%) and phenol (20%). (All percentages are by weight and refer to recovered product.) In the absence of the zeolite no reaction took place. The *p*-AAP may result from acetylation of *p*-HAP either by acetic acid formed by hydrolysis or by direct interaction with the phenyl acetate. The corresponding *ortho*-acetylated phenol was not detected. In contrast to normal Lewis and Bronsted acid catalysed Fries rearrangements under similar conditions there is pronounced *para*-selectivity, the ratio of *para*-products (*p*-HAP + *p*-AAP) to *o*-HAP being *ca* 4.3:1 (with $AlCl_3$ at 165 °C, neat, 70% *ortho*-product is obtained)[1]. Similar results were obtained at 210 °C (Table, entry 4) and in this case there were also traces (*ca* 1%) of 2-methyl-4-oxochromene(1) and 4-methylcoumarin(2). These may result from the facile intramolecular condensation of *o*-acetoxyacetophenone, thus accounting for its absence in the reaction mixture, or by reaction of *o*-HAP with phenyl acetate. Phenol formation can be attributed, at least in part, to the adventitious presence of water, a view supported by an experiment (Table, entry 2) with dried catalyst; this gave less phenol (13% *cf* 20%) but the amount of phenyl acetate converted was also reduced (45% *cf* 70%). It would also be formed as a by-product from the transesterification reaction between phenyl acetate and *p*-HAP.



(p-AAP)



(1)



(2)

Para-selectivity was also observed using H-ZSM-5 (Table, entries 3 and 5). Although the reaction is slower, with only 22% of phenyl acetate consumed after 24h at 170 °C, the preference for *para*-products was slightly greater (6.0:1). The excess phenyl acetate to zeolite (5:1 w/w) used in all the above experiments shows that the process is catalytic. Furthermore, after removal by centrifuging its activity was fully restored by heating at 500 °C for 24h. After 24h at 210 °C using regenerated H-Nu-2 the extent of reaction and product balance were the same, within experimental error, as those for the original sample (Table, entry 6).

When the reaction was repeated using H-Nu-10[8,9] , reported to have the *TON* structure with one-dimensional 5.5 x 4.5 A channels[10] (*cf* H-ZSM-5 which has intersecting 5.4 x 5.6 and 5.1 x 5.5 A channels[11,12]) it proved to be slow and non-selective; after 54h at 210 °C only 12% of the ester had been consumed yielding 10% phenol and 2% of a 1:1 mixture of *ortho*-and *para*-products. As phenyl acetate is too large to enter easily the channels of H-Nu-10 and as there is certainly insufficient void space for the reaction to take place within the zeolite such reaction as occurred must have taken place at the zeolite crystal surface. Using Na-Y, a non-acidic zeolite, some hydrolysis occurred but no rearranged products could be detected (Table, entry 8). It can thus be concluded that for H-Nu-2 and H-ZSM-5 it is the acidic sites that account for the

catalysis and the constraints of the zeolitic void space which give rise to *para*-selectivity.

These results can be compared with those of Olah et al[13] who utilised polymeric perfluorinated resin sulphonic acid (Nafion-H) as a reusable heterogeneous catalyst. Aryl benzoates were converted to *o*- and *p*-hydroxybenzophenones, but they reported that the corresponding reactions with acetate esters were unsuccessful. On re-examining this system we have found that Nafion-H *does* catalyse the Fries rearrangement of phenyl acetate (Table, entry 9). After 24h at 170 °C 83% of the ester had been consumed yielding 10% of a *ca* 1:1 mixture of *o*-HAP and *p*-HAP, together with a large amount of phenol (25%). The zeolites, particularly H-Nu-2 and H-ZSM-5, are therefore of comparable activity to Nafion-H, but in contrast show selectivity in favour of para-substituted products.

There is increasing evidence that zeolites will find widespread use in organic chemistry[14]. The results described in this communication support this view and illustrate one of their most important applications, the enhancement of para-selectivity in aromatic substitution reactions.

Table Influence of zeolites on the Fries rearrangement of phenyl acetate

Entry	Catalyst	Temp. (°C)	Reaction time (h)	Composition of recovered product (weight %) PhOAc	*o*-HAP	*p*-HAP	*p*-AAP	PhOH	*para*:*ortho*
1	H-Nu-2[a]	170	24	30.5	4.3	13.8	4.7	20.5	4.3
2	H-Nu-2(dry)[b]	170	24	55.1	6.2	14.8	2.8	13.2	2.8
3	H-ZSM-5[c]	170	24	77.7	1.1	3.3	3.3	10.8	6.0
4	H-Nu-2	210	24	19.9	4.6	11.7	4.3	20.3	3.5
5	H-ZSM-5	210	24	66.8	3.7	6.0	6.0	13.3	3.2
6	H-Nu-2[d]	210	24	31.7	6.6	13.9[e]		25.2	2.1
7	H-Nu-10[f]	210	54	88.2	1.2	1.3[e]		7.2	1.1
8	Na-Y[g]	170	24	84.8	-[h]	-[h]		17.1	-
9	Nafion-H[i]	170	24	16.9	5.6	4.5[e]		25.2	0.8

[a] supplied by J.L.Casci, ICI Chemicals and Polymers Ltd (Si/Al=13.2)

[b] dried at 400 °C for 17h, stored *in vacuo* over P_2O_5, transferred to reaction flask under dry N_2

[c] synthesised according to EPA42225/1981 (Si/Al = 20.3)

[d] regenerated by heating at 500 °C for 24h

[e] combined yield of *p*-HAP and *p*-AAP

[f] supplied by A.Stewart, ICI Chemicals and Polymers Ltd (Si/Al = 54.5)

[g] from STREM Chemicals Ltd

[h] not detected (<0.1%)

[i] from Aldrich

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